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CELLZOME AG  
Meyerhofstrasse 1  
69117 Heidelberg  
ALLEMAGNE

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Composition of protein complexes of the app-processing pathway

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## 1: FIELD OF THE INVENTION

The present invention relates to protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

## 2. BACKGROUND OF THE INVENTION (cited references are listed in supra)

Alzheimer's disease is a chronic condition that affects millions of individuals worldwide. After onset of the disease sufferers require a high degree of supervision and care. As the proportion of aged individuals in the population increases, the number of sufferers of Alzheimer's disease is expected to expand dramatically. Current top drugs (e.g. Aricept®/donepezil) attempt to achieve a temporary improvement of cognitive functions by inhibiting acetylcholinesterase, which results in increased levels of the neurotransmitter acetylcholine in the brain. These therapies are not suitable for later stages of the disease, they do not treat the underlying disease pathology, and they do not halt disease progression. The growing need for an effective therapy, coupled with the absence of effective treatments, presents a significant opportunity for drug target development and drug discovery.

The brains of sufferers of Alzheimer's disease show a characteristic pathology of prominent neuropathologic lesions, such as the initially intracellular neurofibrillary tangles (NFTs), and the extracellular amyloid-rich senile plaques. These lesions are associated with massive loss of populations of CNS neurons and their progression accompanies the clinical dementia associated with AD. The major component of amyloid plaques is the amyloid beta peptide. Amyloid beta is the proteolytic product of a precursor protein, beta amyloid precursor protein (beta-APP or APP). APP is a type-I trans-membrane protein which is cleaved by several different membrane-associated proteases. The first cleavage of APP occurs extracellularly by one of two proteases, alpha-secretase or beta-secretase. Beta-secretase or BACE1 (beta-site APP-cleaving enzyme) is a type-I transmembrane protein containing an aspartyl protease activity (described in detail below). Alpha secretase is a metalloprotease whose activity is most likely to be provided

by one or a combination of the proteins ADAM10 and ADAM17. Following either the beta or alpha cleavage of APP, the final cleavage event occurs within the membrane and is carried out by a protein complex called gamma secretase. It is the combination of the beta and gamma secretase activities that results in the liberation of the Abeta peptides of 40 and 42 residues (there are also lower levels of other forms) from the APP and ultimately the formation of the amyloid plaques responsible for the pathology of Alzheimer's disease. It is believed that the Abeta-42 peptide is the most critical Abeta species, because it shows the most pronounced neurotoxicity, and can aggregate easily, thus forming a nucleus for the aggregation of other Abeta peptides, such as the Abeta-40 which is typically produced at higher levels than the other species.

The applicant's proprietary proteomics technology (TAP/LC-MS/MS) is particularly successful in the elucidation of membrane protein complexes. These multiprotein complexes form the core of the APP processing pathway and are not amenable to other techniques. Known proteins with an important functional role in APP processing were analysed with The applicant's technology to comprehensively chart the dynamic protein interactions that contribute to Abeta production. Selected novel targets are subsequently validated using cellular or biochemical assays. Moreover, purified multi-protein complexes (e.g. beta- or gamma-secretase) do represent defined functional molecular machines, which are used to evaluate the mechanism of known compounds and for the optimisation of leads.

### **Presenilins**

Presenilins 1 and 2 (PS1 and PS2) are integral membrane proteins which are localised in the endoplasmic reticulum, the Golgi and also at the cell surface (1). They are predominantly found as a heterodimers of the NTF and CTF endoproteolytic fragments. The protease that cleaves presenilins (the "presenilinase") is not known, it is likely that the process is autocatalytic, also the functional significance of PS (auto)proteolysis is unclear.

Presenilins are involved in the proteolytical processing of Amyloid precursor protein (APP) (2,3) and the Notch receptor (4,5). In addition, Presenilins are associated with the cell-adhesion proteins alpha and beta-catenin, N-cadherin, and E-cadherin (6) (7) and other members of the armadillo family (8) (9) (10) (11).

APP processing by Presenilins is through their effects on gamma-secretase which cleaves APP, generating the C-terminus of the A-beta peptide. PS1 associates with the C83 and C99 processed C-terminal fragments of APP (12), Nicastrin (13) and Pen-2 (14). Aph-1 (15) (14) is required in Presenilin processing. It is not clear whether Presenilins regulate gamma-secretase activity directly or whether they are protease enzymes themselves (16). The gamma secretase activity could comprise a multimeric complex of these proteins (13) (17) but it is not known how the relationship between these proteins affects secretase activity.

Familial Alzheimer's disease (FAD) patients carry mutations in the presenilin proteins (PS1; PS2) or in APP. These mutations result in increased production of A-beta42 (18) which is the main component of cerebral plaques in FAD (19).

Understanding the composition of the gamma-secretase complex, the relationship between its component parts and its regulation are important in the design of drugs for use in Alzheimer's disease patients.

### **Nicastrin**

Nicastrin is a type 1 trans-membrane glycoprotein with a conserved transmembrane domain and DYIGS motif (13) which is constitutively expressed in neural cell lines (20). Biochemical studies have shown that Nicastrin binds to Presenilins 1 and 2, C-terminal derivatives of APP (13), membrane-tethered forms of Notch (21) and that it is a member of the gamma-secretase complex along with PS1 and PS2 (17). Gamma secretase activity is involved in the cleavage of both Notch and APP. It has been shown that Nicastrin is required for the intra-membrane cleavage of Notch (22) and APP (23), it may also have a role in post-translational stabilisation of Presenilin (24).

Aph-1 (15) and Pen-2 (14) were cloned recently in a screen for presenilin enhancers ("pen") in *C. elegans* and shown to interact genetically with Aph-2 (Nicastrin). Defects in Aph-1 affect Notch signalling and Nicastrin localisation (15). Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins. Francis et al. (14) cloned the putative human orthologues of these genes, Aph-1a, Aph-1b and Pen-2, and recently Lee et al. (25) also cloned the human Aph-1 cDNAs.

The exact components of the gamma-secretase complex are not known but these two novel proteins could be components of or accessory factors to the complex and may interact together directly with Presenilin or with a Presenilin/Nicastrin complex. Nicastrin



is therefore a member of the active gamma-secretase complex and there is recent evidence that it is the fully glycosylated form of the protein which is important in this complex. (26-30)

### **Aph-1**

Goutte et al. (15) cloned aph-1 from *C. elegans*. Aph-1 encodes a novel conserved membrane protein with seven hydrophobic regions which are predicted to be membrane spanning. It has a 40 amino acid hydrophilic tail. *C. elegans* aph1 mutants have a phenotype which is indicative of a defect in Notch signalling. In these mutants, Aph-2 (Nicastrin) localisation is altered from being at the cell surface to being in the cytoplasm, concentrated around the nucleus. In *C. elegans*, Aph-1 interacts genetically with Aph-2 (Nicastrin) and Sel-12 (one of the *C. elegans* Presenilin genes) (14).

There are Human, Mouse, *Drosophila* Aph-1 homologues which are potential orthologues. Recently, the human Aph-1 homologues, hAph-1a and hAph-1b have been cloned (14,25). Aph-1a, the hypothetical CGI-78 protein, and Sambiasin (European Patent Application 02014244.4 are all products of the same gene. Francis et al (14) showed that Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured *Drosophila* cells.

Lee et al. (25) cloned two splice variants of Aph-1a called Aph-1aS and Aph-1aL and Aph-1b. They have shown that mammalian Aph-1aL associates with Nicastrin and PS1 NTF/CTF heterodimers and with PS2 and Nicastrin in cultured cells and that endogenous Aph1aL associates with Nicastrin and PS1 in rat brain. Inhibition of the expression of Aph1a reduces the expression of both PS1 and PS2 but not Nicastrin and results in the accumulation of gamma-secretase substrates and the reduction of Aβ. Aph1a was also shown to be required for Notch cleavage.

Aph-1 may have a role in the maturation and trafficking of Nicastrin but it is necessary for gamma-secretase function and may be a member of the gamma-secretase complex.

### **Pen-2**

Francis et al. (14) isolated pen-1 and pen-2 as two presenilin enhancer genes in a genetic screen in *C. elegans*. Pen-1 is identical to Aph-1 (15). Pen-2 has two transmembrane domains and is thought to be a polytopic integral membrane protein. This group cloned the human homologues of Aph-1 and Pen-2. In *C. elegans*, Aph-1 and

Pen-2 interact genetically with Aph-2 (Nicastrin) but not with each other. Hop-1 and Sel-12 are the *C.elegans* presenilin genes. Aph-2 interacts with Hop-1 whereas Aph-1 and Pen-2 interact with Sel-12 (14).

Pen-2 associates with PS1, PS2 and Nicastrin in mammalian cells and Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured *Drosophila* cells (14).

Nicastrin maturation is affected by the levels of PS1 and Pen-2. Loss of PS1 or a reduction in expression of Nicastrin reduces Pen-2 protein levels and a reduction in expression of Pen-2 decreases levels of both PS1, PS2 proteins. In addition, reducing the expression of Pen-2 by RNAi reduces the level of the PS1 complex (31). These data suggest that Pen-2 is either a component of or regulates the assembly of the PS1 complex and that the expression of these proteins is co-ordinately regulated.

### **BACE1 (beta-secretase)**

Vassar et al. (32) cloned a transmembrane aspartic protease that had the characteristics of the postulated beta-secretase of APP. Three other groups also cloned BACE1 using different approaches. BACE1 knockout mice have a normal phenotype, suggesting that therapeutic inhibition of BACE1 for AD may be free of mechanism-based toxicity. BACE1 <sup>-/-</sup> mice who are also homozygous for an amyloid precursor protein transgene lack brain beta-amyloid and beta-secretase-cleaved APP C-terminal fragments. (33). Brain and primary cortical cultures from BACE1 knockout mice showed no detectable beta-secretase activity, and primary cortical cultures from BACE knockout mice produced much less amyloid-beta from APP. This suggests that BACE1, rather than its paralogue BACE2, is the main beta-secretase for APP.

BACE1 is a protein of 501 amino acids containing a 21-aa signal peptide followed by a proprotein domain spanning aa 22 to 45. There are alternatively spliced forms, BACE-I-457 and BACE-I-476. The luminal domain of the mature protein is followed by one predicted transmembrane domain and a short cytosolic C-terminal tail of 24 aa. BACE1 is predicted to be a type 1 transmembrane protein with the active site on the luminal side of the membrane, where beta-secretase cleaves APP and possible other yet unidentified substrates. BACE1 mRNA in rat brain is present at higher levels in neurons than in glia, supporting that neurons are the primary source of the extracellular A-beta deposited in plaques. Sequence and mass spectrometry analyses showed that asn153, asn172, asn223, and asn354 of the BACE1 ectodomain are N-glycosylation

sites. In addition, the ectodomain contains 6 cys residues that form disulfide bridges between positions 216 and 420, 278 and 443, and 330 and 380. The C-terminal domain of BACE1 contains a dileucine motif (LL499/500) that can potentially regulate its trafficking and endocytosis, and an adjacent serine, which is a casein kinase 1 phosphorylation site (S498) (34). The propeptide is predominantly cleaved from BACE1 by furin (35). In cells expressing wt or Swedish mutant APP, transient overexpression of BACE1 decreased alpha-secretase cleavage and increased beta-secretase activity at the known beta-secretase positions, asp1 and glu11. Although BACE1 is clearly a key enzyme required for the processing of APP into Ab, other potential substrates and functions of BACE1 are unknown. Also, no BACE1 interacting proteins with regulatory or modulatory functions have been described. Proteins that activate BACE1 activity would form suitable intervention points for Alzheimer's disease therapy. In addition, proteins that inhibit BACE1, like substrates or pseudosubstrates, could also provide suitable means of intervention e.g. as proteins therapeutics.

#### **APP and the beta-CTF ("C99")**

APP is the precursor of Abeta, a peptide which forms the principal component of Alzheimer disease (AD) senile plaques (3) Masters et al. purified the cerebral amyloid protein that forms the plaque core in AD and Down syndrome. Van Nostrand et al. (36) presented evidence that nexin-II, a protease inhibitor that is synthesized and secreted by extravascular cells, is identical to APP. Multhaup et al. (37) demonstrated that APP is involved in copper reduction. They postulated that copper-mediated toxicity may contribute to neurodegeneration in AD, possibly by increased production of hydroxyl radicals. Yan et al. (38) reported that the receptor for advanced glycation end products RAGE is a receptor for the a-beta peptide and that expression of this receptor increases in AD. Expression of RAGE is particularly increased in neurons close to deposits of amyloid beta peptide and to neurofibrillary tangles. Kaneko et al. (39) demonstrated that nanomolar concentrations of various synthetic beta amyloids specifically impaired mitochondrial succinate dehydrogenase, and speculated that one of the primary targets of beta amyloids is the mitochondrial electron transport chain.

Several missense mutations in the APP gene have been identified that result in early-onset AD: the Swedish APP670/671 double mutation; 3 different mutations at codon 717: the London APP717 mutation, V717I, V717F, and V717G; and the Florida APP716 mutation (Reviewed by Bertram and Tanzi (40)). Most of these AD-related



mutations involve amino acid changes near the beta- and gamma-secretase cleavage sites. Two other missense mutations in the APP gene are located within A-beta near the alpha-secretase cleavage site: the Flemish APP692 mutation, which is associated with cerebral hemorrhage due to congophilic amyloid angiopathy or with early-onset AD with onset age in the mid-forties; and the Dutch APP693 mutation. Almost all AD-linked mutations do elevate secretion of A-beta-42, however, APP693 does not. (41)

Cao and Sudhof (42) demonstrated that the cytoplasmic tail of APP forms a complex with the nuclear adaptor protein Fe65 and the histone acetyltransferase TIP60. This complex stimulates transcription via heterologous Gal4 or LexA DNA binding domains, suggesting that release of the cytoplasmic tail of APP by gamma-cleavage may function in gene expression. The complex could modify expression of genes that function in inflammation (43) or apoptosis (44).

Weggen et al. (45) reported that the nonsteroidal antiinflammatory drugs ibuprofen, indomethacin, and sulindac can decrease the levels of high amyloidogenic amyloid-beta-42 peptide produced from a variety of cultured cells by as much as 80%. This effect was not seen in all NSAIDs and seemed not to be mediated by inhibition of cyclooxygenase (Cox) activity. Weggen et al. (2001) also demonstrated that short-term administration of ibuprofen to mice that produce APP lowered their brain levels of amyloid-beta-42. In cultured cells, the decrease in amyloid-beta-42 secretion was accompanied by an increase in the amyloid-beta(1-38) isoform, indicating that NSAIDs subtly alter gamma-secretase activity without significantly perturbing other APP processing pathways or Notch cleavage.

Proteins and other factors that regulate APP processing, and especially those that influence levels of Abeta-42 versus other Abeta species, form important potential targets in AD therapy.

### **Calsenilin**

In a yeast two-hybrid screen with the C-terminus of Presenilin 2, a neuronal EF-hand (calcium-binding) protein was identified and named "calsenilin" (46). It interacted with both Presenilin 1 and Presenilin 2 in cells and regulated the levels of a proteolytic product of Presenilin 2. Calsenilin is identical to KChIP3, a protein which was found in a yeast two-hybrid screen for proteins interacting with A-type potassium channels (Kv4.3) (47). KChIP3 i) increased the density of Kv4.2 currents indicating a stabilisation of the

channels at the plasma membrane; ii) shifted the current to hyperpolarized potentials; iii) slowed down the kinetics of inactivation and increased the kinetics of recovery. Calsenilin is also identical to the transcriptional repressor DREAM which acts constitutively to suppress prodynorphin expression in spinal cord neurons (48). Knocking out DREAM results in sufficient dynorphin expression to produce a strong reduction in generalized pain behavior, highlighting the role that intracellular molecules play in modulating pain gating in the spinal cord. Hence proteins that modulate Calsenilin/DREAM activity are interesting targets in nociception.

### **Tau**

Neurofibrillary tangles (NFT), intraneuronal tau protein deposits, are hallmarks of several neurodegenerative disorders such as Alzheimer's and Pick's disease, frontotemporal dementia, cortico-basal degeneration and progressive supranuclear palsy.

The seven tau isoforms are all products of a single gene. Alternative splicing gives rise to six mRNA species differentially expressed in the CNS, depending on stage of neuronal maturation and neuron type. Tau is found mainly in the axon whereas a related protein, MAP2, is mainly found in dendrites.

Tau and MAP2 are microtubule-associated proteins (MAPs) which coassemble with microtubules and colocalise with microtubules in cells. Tau is a nonstructured molecule with a microtubule binding site containing 3 or 4 characteristic amino acid repeat in its carboxyl-terminal half. Alonso et al. (49) noted that in the brains of AD patients the neuronal cytoskeleton is progressively disrupted and replaced by tangles of paired helical filaments (PHFs), and that PHFs are composed mainly of hyperphosphorylated forms of tau. They demonstrated that in solution normal tau associated with the hyperphosphorylated AD P-tau to form large tangles of filaments. They also demonstrated that dephosphorylation with alkaline phosphatase abolished the ability of AD P-tau to aggregate in vitro. In a form of autosomal dominant inherited dementia known as FTDP17 or Pick disease, the tau gene carries missense mutations or mutations in the 5'- splice site of exon 10, which results in increased levels of tau isoforms with 4 microtubule-binding repeats. These mutations lead to tau molecules that show reduced affinity for microtubules or are more prone to self aggregation.

Proteins and other factors that influence the affinity of tau protein for microtubules, and moreover, influence the aggregation of tau, which is probably mediated by

phosphorylation and dephosphorylation events, are important potential targets in AD therapy.

### **Fe65**

Fe65 is a PTB domain- and WW domain-containing adaptor protein that is part of protein complexes at the plasma membrane as well as in the nucleus: It interacts with the Alzheimer's disease amyloid precursor protein (APP; (50)) and related proteins APLP1 and APLP2 (51). Binding of Fe65 to the cytoplasmic tail of APP enhances production of amyloid-forming Abeta peptides (52), but the molecular mechanism of this amyloidogenic effect of Fe65 has not been elucidated. Furthermore, Fe65 stabilizes APP intracellular domain (AICD) (APP intracellular domain (AICD)), the cytosolic product of APP cleavage by gamma-secretase, (53) and forms a nuclear protein complex with TIP60 (42). Little is known about the functional consequences of Fe65-dependent transactivation. The important role of TIP60 in interleukin-1beta- and NF-KappaB-dependent transactivation (43) suggests, however, that the Fe65 complex might function in inflammation.

Fe65 has been shown to bind to the transcription factor CP2/LSF/LBP1 (54) and the low-density lipoprotein receptor-related protein (55), but the significance of these interactions is unknown. Finally, Fe65 has been observed to block cell cycle progression by downregulating thymidylate synthase expression via an unknown mechanism (56).

Understanding the composition of the Fe65 complex, the relationship between its component parts and its regulation might therefore be important in the design of drugs for use in Alzheimer's disease patients as well as for the treatment of various inflammatory conditions and cancer.

### **X11beta**

X11beta/Mint-2 is a neuronal adaptor protein that is believed to be involved in signal transduction processes. It is also regarded as a putative vesicular trafficking protein in the brain that can form a complex with the potential to couple synaptic vesicle exocytosis to neuronal cell adhesion (57).

X11beta interacts with the Alzheimer's disease amyloid precursor protein (APP) (50). Acting synergistically with Munc18a (58), X11beta stabilises APP and inhibits production of proteolytic APP fragments including the A beta peptide that is deposited in the brains of Alzheimer's disease patients (59).

Via a mechanism that depends on its PDZ domain (yet has otherwise not been characterized), X11beta potently inhibits transactivation by an APP-Gal4/VP16 fusion protein (58). Besides interacting with APP, X11beta binds to the C-terminus of presenilin1, although not as strongly as does X11alpha (58). In addition, X11beta has been reported to interact with XB51 (60), but the functional significance of this interaction is unknown.

In *Drosophila*, dX11beta overexpression in eye imaginal disks causes disruption of compound eye morphology due to enhanced apoptosis of neuronal cells (61). X11beta has been shown to bind to NF-KappaB-p65 through its PDZ domain. This interaction has been implicated in NF-KappaB-dependent Abeta 1-42 production (62).

Elucidation of X11beta complex composition and regulation might therefore help develop novel ways of therapeutic intervention in Alzheimer's disease and inflammation.

### 3. SUMMARY OF THE INVENTION

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative



thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and  
 (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;  
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.
5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:  
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X

SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
  - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
  - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
  - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
18. A kit comprising in one or more containers:
  - (a) the complex of any of No. 1 - 8 and/or the proteins of No. 13 and/or
  - (b) an antibody according to No. 17 and/or



- (c) a nucleic acid encoding a protein of the complex of any of No. 1 – 8 and/or a protein of No. 13 and/or
- (d) cells expressing the complex of any of No. 1 – 8 and/or a protein of No. 13 and, optionally,
- (e) further components such as reagents, buffers and working instructions.

19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
21. Array, preferably a microarray, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for modifying a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex of any of No. 1 - 8 with said substrate, such that said substrate is modified.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or a protein according to No. 13.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of No. 1 - 8 and/or a protein of No. 13, comprising the following steps:
  - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
  - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.

31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
41. The complex of any one of No. 1 - 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

### 3.1 DEFINITIONS

The term "activity" as used herein, refers to the function of a molecule in its broadest sense. It generally includes, but is not limited to, biological, biochemical, physical or chemical functions of the molecule. It includes for example the enzymatic activity, the ability to interact with other molecules and ability to activate, facilitate, stabilize, inhibit, suppress or destabilize the function of other molecules, stability, ability to localize to certain subcellular locations. Where applicable, said term also relates to the function of a protein complex in its broadest sense.

The term "agonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, increases the amount of, or prolongs the duration of, the activity of the complex. The stimulation may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Agonists may include proteins, nucleic acids, carbohydrates or any other organic or inorganic molecule or metals. Agonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred activators are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 25%, at least 50%, at least 100%, at least, 200%, at least 500% or at least 1000% at a concentration of the activator  $1\mu\text{g ml}^{-1}$ ,  $10\mu\text{g ml}^{-1}$ ,  $100\mu\text{g ml}^{-1}$ ,  $500\mu\text{g ml}^{-1}$ ,  $1\text{mg ml}^{-1}$ ,  $10\text{mg ml}^{-1}$  or  $100\text{mg ml}^{-1}$ . Any combination of the



above mentioned degrees of percentages and concentration may be used to define an agonist of the invention, with greater effect at lower concentrations being preferred.

The term "amount" as used herein and as applicable to the embodiment described relates to the amount of the particular protein or protein complex described, including the value of null, i.e. where no protein or protein complex described in that particular embodiment is present under the or any of the conditions which might be specified in that particular embodiment.

The term "animal" as used herein includes, but is not limited to mammals, preferably mammals such as cows, pigs, horses, mice, rats, cats, dogs, sheep, goats and most preferably humans. Other animals used in agriculture, such as chickens, ducks etc. are also included in the definition as used herein.

The term "animal" as used herein does not include humans if being used in the context of genetic alterations to the germline.

The term "antagonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, decreases the amount of, or the duration or level of activity of the complex. The effect may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Antagonists may include proteins, including antibodies, nucleic acids, carbohydrates or any other organic or inorganic molecule or metals. Antagonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred antagonists are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 20%, at least 30%, at least 40% at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 99% at a concentration of the inhibitor of  $1\mu\text{g ml}^{-1}$ ,  $10\mu\text{g ml}^{-1}$ ,  $100\mu\text{g ml}^{-1}$ ,  $500\mu\text{g ml}^{-1}$ ,  $1\text{mg ml}^{-1}$ ,  $10\text{mg ml}^{-1}$  or  $100\text{mg ml}^{-1}$ .

Any combination of the above mentioned degrees of percentages and concentration may be used to define antagonist of the invention, with greater effect at lower concentrations being preferred.

The term "antibodies" as used herein, include include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library.

The term "binding" as used herein means a stable or transient association between two molecules, including electrostatic, hydrophobic, ionic and/or hydrogen-bond interaction under physiological conditions and/or conditions being used in diagnostic or prognostic method or process or procedure.

The term "carrier" as used herein refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

If not stated otherwise, the terms "complex" and "protein complex" are used interchangeably herein and refer to a complex of proteins that is able to perform one or more functions of the wild type protein complex. The protein complex may or may not include and/or be associated with other molecules such as nucleic acid, such as RNA or

DNA, or lipids or further cofactors or moieties selected from a metal ions, hormones, second messengers, phosphate, sugars.

A "complex" of the invention may also be part of or a unit of a larger physiological protein assembly.

The term "component of the APP processing pathway" as used herein refers to a protein and/or protein complex which is involved in mediating APP processing in a cell. Components of the APP processing pathway include the following protein complexes as provided herein and components thereof:

Aph1a-complex, APP-695SW-complex, APP-C99-complex, Fe65-complex, Nicastrin-complex, Psen-2-complex, Pen2-complex, Tau-complex, X11 $\beta$ -complex

If not stated otherwise, the term "compound" as used herein are include but are not limited to peptides, nucleic acids, carbohydrates, natural product extract librariesorganic molecules, preferentially small organic molecules, anorganic molecules, including but not limited to chemicals, metals and organometallic molecules.

The terms "derivatives" or "analogs of component proteins" or "variants" as used herein include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions. It means a protein which is the outcome of a modification of the naturally occurring protein, by amino acid substitutions, deletions and additios, respectively, which derivatives still exhibit the biological function of the naturally occurring protein although not necessarily to the same degree. The biological function of such proteins can e.g. be examined by suitable available in vitro assays as provided in the invention.

The term "functionally active" as used herein refers to a polypeptide, namely a fragment or derivative, having structural, regulatory, or biochemical functions of the protein according to the embodiment of which this polypeptide, namely fragment or derivative is related to.

The term "fragment" as used herein refers to a polypeptide of at least 10, 20, 30, 40 or 50 amino acids of the component protein according to the embodiment. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids.



The term "gene" as used herein refers to a nucleic acid comprising an open reading frame encoding a polypeptide of, if not stated otherwise, the present invention, including both exon and optionally intron sequences.

The terms "homologue" or "homologous gene products" as used herein mean a protein in another species, preferably mammals, which performs the same biological function as the a protein component of the complex further described herein. Such homologues are also termed "orthologous gene products". The algorithm for the detection of orthologue gene pairs from humans and mammals or other species uses the whole genome of these organisms. First, pairwise best hits are retrieved, using a full Smith-Waterman alignment of predicted proteins. To further improve reliability, these pairs are clustered with pairwise best hits involving *Drosophila melanogaster* and *C. elegans* proteins. Such analysis is given, e.g., in *Nature*, 2001, 409:860-921. The homologues of the proteins according to the invention can either be isolated based on the sequence homology of the genes encoding the proteins provided herein to the genes of other species by cloning the respective gene applying conventional technology and expressing the protein from such gene, or by isolating proteins of the other species by isolating the analogous complex according to the methods provided herein or to other suitable methods commonly known in the art.

The term "host cells" or, were applicable, "cells" or "hosts" as used herein is intended to be understood in a broadest sense and include, but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used. It is understood that this term not only refers to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

The term "modification" as used herein refers to all modifications of a protein or protein complex of the invention including cleavage and addition or removal of a group.

The term "nucleic acid" as used herein refers to polynucleotides such as deoxyribonucleic acid (DNA), and, where appropriate, ribonucleic acid (RNA). They may

also be polynucleotides which include within them synthetic or modified nucleotides. A number of different types of modification to polynucleotides are known in the art. These include methylphosphonate and phosphorothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. For the purposes of the present invention, it is to be understood that the polynucleotides described herein may be modified by any method available in the art. Such modifications may be carried out in order to enhance the in vivo activity or lifespan of polynucleotides of the invention. Polynucleotides according to the invention may be produced recombinantly, synthetically, or by any means available to those of skill in the art. They may also be cloned by standard techniques. The polynucleotides are typically provided in isolated and/or purified form. As applicable to the embodiment being described, they include both single stranded and double-stranded polynucleotides.

The term "percent identity", as used herein, means the number of identical residues as defined by an optimal alignment using the Smith-Waterman algorithm divided by the length of the overlap multiplied by 100. The alignment is performed by the search program (Pearson, 1991, Genomics 11:635-650) with the constraint to align the maximum of both sequences.

The terms "polypeptides" and "proteins" are, where applicable, used interchangeably herein. They may be chemically modified, e.g. post-translationally modified. For example, they may be glycosylated or comprise modified amino acid residues. They may also be modified by the addition of a signal sequence to promote their secretion from a cell where the polypeptide does not naturally contain such a sequence. They may be tagged with a tag. They may be tagged with different labels which may assist in identification of the proteins in a protein complex. Polypeptides/proteins for use in the invention may be in a substantially isolated form. It will be understood that the polypeptid/protein may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide/protein for use in the invention may also be in a substantially purified form, in which case it will generally comprise the polypeptide in a preparation in which more than 50%, e.g. more than 80%, 90%, 95% or 99%, by weight of the polypeptide in the preparation is a polypeptide of the invention.

"Target for therapeutic drug" means that the respective protein (target) can bind the active ingredient of a pharmaceutical composition and thereby changes its biological activity in response to the drug binding.

The term "tag" as used herein is meant to be understood in its broadest sense and to include, but is not limited to any suitable enzymatic, fluorescent, or radioactive labels and suitable epitopes, including but not limited to HA-tag, Myc-tag, T7, His-tag, FLAG-tag, Calmodulin binding proteins, glutathione-S-transferase, strep-tag, KT3-epitope, EEF-epitopes, green-fluorescent protein and variants thereof.

The term "therapeutics" as used herein, includes, but is not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments); antibodies thereto; nucleic acids encoding the component protein, and analogs or derivatives thereof; component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The term "vector" as used herein means a nucleic acid molecule capable of transporting another nucleic acid sequence to which it has been linked. Preferred vectors are those capable of autonomous replication and/or expression of nucleic acids to which they linked. The terms "plasmid" and "vector" are used interchangeably herein when applicable to the embodiment. However, vectors other than plasmids are also included herein. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

#### 4. DETAILED DESCRIPTION OF THE INVENTION

##### Overview:

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said protein complex were identified. The components are listed in table 1.

Said object is further achieved by the characterisation of component proteins. These proteins are listed in table 2.

The invention thus relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
  - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-



stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;  
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the

complex comprises at least one protein selected from table 1, fifth column of a given complex.

5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:  
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.

13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
  - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
  - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
  - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
18. A kit comprising in one or more containers:
- (a) the complex of any of No. 1 - 8 and/or the proteins of No. 13 and/or
  - (b) an antibody according to No. 17 and/or
  - (c) a nucleic acid encoding a protein of the complex of any of No. 1 - 8 and/or a protein of No. 13 and/or
  - (d) cells expressing the complex of any of No. 1 - 8 and/or a protein of No. 13 and, optionally,
  - (e) further components such as reagents, buffers and working instructions.
19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
21. Array, preferably a microarray, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for modifying a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex of any of No. 1 - 8 with said substrate, such that said substrate is modified.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or a protein according to No. 13.



24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of No. 1 - 8 and/or a protein of No. 13, comprising the following steps:
- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
  - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or

disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
41. The complex of any one of No. 1 - 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

Animal models are also provided herein.

Preferably, the protein components of the complexes described herein are all mammalian proteins. The complexes can also consist only of the respective homologues from other mammals such as mouse, rat, pig, cow, dog, monkey, sheep or horse or other species such as *D. melanogaster*, *C. elegans* or chicken. In another preferred embodiment, the complexes are a mixture of proteins from two or more species.

## TABLES:

### Table 1: Composition of Complexes

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Entry point'): Lists the bait proteins that have been chosen for the purification of the given complex.

Third column ('All interactors'): Lists all novel interactors which have been identified as members of the complex and all interactors which have been known to be associated with the bait so far.

Fourth column ('Known interactors'): Lists all interactors which have been known to be associated with the bait so far.

Fifth column ('Novel interactors of the complex'): Lists all novel interactors of the complex which have been identified in the experiments provided herein.

Sixth column: Separately lists the members of the newly identified complex which have not been annotated previously.

#### Table 2: Individual Proteins of the Complexes

First column ('Protein'): Lists in alphabetical order all proteins which have been identified as interactors of the complexes presented herein.

Second column ('SEQ ID'): Lists the SEQ ID (Sequence Identifications) of the proteins herein as used herein.

Third column ('IPI-Numbers'): Lists the IPI-Numbers of the proteins herein. The IPI-Numbers refer to the International Protein Index created by the European Bioinformatics Institute (EMBL-EBI), Hinxton, UK.

Fourth column ('Molecular Weight'): Lists the Molecular Weight of the proteins in Dalton.

#### Table 3: Biochemical Activities of the Complexes of the invention.

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Biochemical Activity'): Lists biochemical activities of the complexes. Assays in order to test these activities are also provided herein (infra).

#### Table 4: Medical Applications of the Complexes of the invention

First column ('Name of complex'): Lists the name of the protein complexes as used herein

Second column ('Medical application'): lists disorder, diseases, disease areas etc. which are treatable and/or preventable and/or diagnosable etc. by therapeutics and methods interacting with/acting via the complex.

### 4.1 PROTEIN COMPLEXES/PROTEINS OF THE INVENTION



The protein complexes of the present invention and their component proteins are described in the Tables 1 - 4. The protein complexes and component proteins can be obtained by methods well known in the art for protein purification and recombinant protein expression. For example, the protein complexes of the present invention can be isolated using the TAP method described in Section 5, *infra*, and in WO 00/09716 and Rigaut et al., 1999, *Nature Biotechnol.* 17:1030-1032, which are each incorporated by reference in their entirety. Additionally, the protein complexes can be isolated by immunoprecipitation of the component proteins and combining the immunoprecipitated proteins. The protein complexes can also be produced by recombinantly expressing the component proteins and combining the expressed proteins.

The nucleic and amino acid sequences of the component proteins of the protein complexes of the present invention are provided herein (SEQ ID NO 1 - 315), and can be obtained by any method known in the art, e.g., by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of each sequence, and/or by cloning from a cDNA or genomic library using an oligonucleotide specific for each nucleotide sequence.

Homologues (e.g., nucleic acids encoding component proteins from other species) or other related sequences (e.g., variants, paralogs) which are members of a native cellular protein complex can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular nucleic acid sequence as a probe, using methods well known in the art for nucleic acid hybridization and cloning.

Exemplary moderately stringent hybridization conditions are as follows: prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 µg/ml denatured salmon sperm DNA and 5-20 X 10<sup>6</sup> cpm of <sup>32</sup>P-labeled probe. Washing of filters is done at 37°C for 1 hour in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 °C for 45 min before autoradiography. Alternatively, exemplary conditions of high stringency are as follows: e.g., hybridization to filter-bound DNA in 0.5 M NaHPO<sub>4</sub>, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at 68°C (Ausubel et al., eds., 1989, *Current Protocols in Molecular Biology*, Vol. 1, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Other conditions of high stringency which may be

used are well known in the art. Exemplary low stringency hybridization conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100  $\mu$ g/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

For recombinant expression of one or more of the proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protein can be inserted into an appropriate expression vector, i.e., a vector that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals can also be supplied by the native promoter of the component protein gene, and/or flanking regions.

A variety of host-vector systems may be utilized to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

In a preferred embodiment, a complex of the present invention is obtained by expressing the entire coding sequences of the component proteins in the same cell, either under the control of the same promoter or separate promoters. In yet another embodiment, a derivative, fragment or homologue of a component protein is recombinantly expressed. Preferably the derivative, fragment or homologue of the protein forms a complex with the other components of the complex, and more preferably forms a complex that binds to an anti-complex antibody. Such an antibody is further described *infra*.

Any method available in the art can be used for the insertion of DNA fragments into a vector to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and protein coding sequences. These methods may include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombinant techniques (genetic recombination). Expression of nucleic acid

sequences encoding a component protein, or a derivative, fragment or homologue thereof, may be regulated by a second nucleic acid sequence so that the gene or fragment thereof is expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins may be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the gene for the component protein. Promoters that may be used can be selected from among the many known in the art, and are chosen so as to be operative in the selected host cell.

In a specific embodiment, a vector is used that comprises a promoter operably linked to nucleic acid sequences encoding a component protein, or a fragment, derivative or homologue thereof, one or more origins of replication, and optionally, one or more selectable markers (e.g., an antibiotic resistance gene).

In another specific embodiment, an expression vector containing the coding sequence, or a portion thereof, of a component protein, either together or separately, is made by subcloning the gene sequences into the EcoRI restriction site of each of the three pGEX vectors (glutathione S-transferase expression vectors; Smith and Johnson, 1988, Gene 7:31-40). This allows for the expression of products in the correct reading frame.

Expression vectors containing the sequences of interest can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene function, and (c) expression of the inserted sequences. In the first approach, coding sequences can be detected by nucleic acid hybridization to probes comprising sequences homologous and complementary to the inserted sequences. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" functions (e.g., resistance to antibiotics, occlusion body formation in baculovirus, etc.) caused by insertion of the sequences of interest in the vector. For example, if a component protein gene, or portion thereof, is inserted within the marker gene sequence of the vector, recombinants containing the encoded protein or portion will be identified by the absence of the marker gene function (e.g., loss of  $\beta$ -galactosidase activity). In the third approach, recombinant expression vectors can be identified by assaying for the component protein expressed by the recombinant vector. Such assays can be based, for example, on the physical or functional properties of the interacting species in in vitro assay systems, e.g., formation of a complex comprising the protein or binding to an anti-complex antibody.



Once recombinant component protein molecules are identified and the complexes or individual proteins isolated, several methods known in the art can be used to propagate them. Using a suitable host system and growth conditions, recombinant expression vectors can be propagated and amplified in quantity. As previously described, the expression vectors or derivatives which can be used include, but are not limited to, human or animal viruses such as vaccinia virus or adenovirus; insect viruses such as baculovirus, yeast vectors; bacteriophage vectors such as lambda phage; and plasmid and cosmid vectors.

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or modifies or processes the expressed proteins in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically-engineered component proteins may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation, etc.) of proteins. Appropriate cell lines or host systems can be chosen to ensure that the desired modification and processing of the foreign protein is achieved. For example, expression in a bacterial system can be used to produce an unglycosylated core protein, while expression in mammalian cells ensures "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

In other specific embodiments, a component protein or a fragment, homologue or derivative thereof, may be expressed as fusion or chimeric protein product comprising the protein, fragment, homologue, or derivative joined via a peptide bond to a heterologous protein sequence of a different protein. Such chimeric products can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acids to each other by methods known in the art, in the proper coding frame, and expressing the chimeric products in a suitable host by methods commonly known in the art. Alternatively, such a chimeric product can be made by protein synthetic techniques, e.g., by use of a peptide synthesizer. Chimeric genes comprising a portion of a component protein fused to any heterologous protein-encoding sequences may be constructed.

In particular, protein component derivatives can be made by altering their sequences by substitutions, additions or deletions that provide for functionally equivalent molecules. Due to the degeneracy of nucleotide coding sequences, other DNA

sequences that encode substantially the same amino acid sequence as a component gene or cDNA can be used in the practice of the present invention. These include but are not limited to nucleotide sequences comprising all or portions of the component protein gene that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change. Likewise, the derivatives of the invention include, but are not limited to, those containing, as a primary amino acid sequence, all or part of the amino acid sequence of a component protein, including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity that acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

In a specific embodiment, up to 1%, 2%, 5%, 10%, 15% or 20% of the total number of amino acids in the wild type protein are substituted or deleted; or 1, 2, 3, 4, 5, or 6 or up to 10 or up to 20 amino acids are inserted, substituted or deleted relative to the wild type protein.

In a specific embodiment of the invention, the nucleic acids encoding a protein component and protein components consisting of or comprising a fragment of or consisting of at least 6 (continuous) amino acids of the protein are provided. In other embodiments, the fragment consists of at least 10, 20, 30, 40, or 50 amino acids of the component protein. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids. Derivatives or analogs of component proteins include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of



hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions.

In a specific embodiment, proteins are provided herein, which share an identical region of 20, 30, 40, 50 or 60 contiguous amino acids of the proteins listed in table 2.

The protein component derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations which result in their production can occur at the gene or protein level. For example, the cloned gene sequences can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, *Molecular Cloning, A Laboratory Manual*, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The sequences can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated in vitro. In the production of the gene encoding a derivative, homologue or analog of a component protein, care should be taken to ensure that the modified gene retains the original translational reading frame, uninterrupted by translational stop signals, in the gene region where the desired activity is encoded.

Additionally, the encoding nucleic acid sequence can be mutated in vitro or in vivo, to create and/or destroy translation, initiation, and/or termination sequences, or to create variations in coding regions and/or form new restriction endonuclease sites or destroy pre-existing ones, to facilitate further in vitro modification. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis and in vitro site-directed mutagenesis (Hutchinson et al., 1978, *J. Biol. Chem.* 253:6551-6558), amplification with PCR primers containing a mutation, etc.

Once a recombinant cell expressing a component protein, or fragment or derivative thereof, is identified, the individual gene product or complex can be isolated and analyzed. This is achieved by assays based on the physical and/or functional properties of the protein or complex, including, but not limited to, radioactive labeling of the product followed by analysis by gel electrophoresis, immunoassay, cross-linking to marker-labeled product, etc.

The component proteins and complexes may be isolated and purified by standard methods known in the art (either from natural sources or recombinant host cells expressing the complexes or proteins), including but not restricted to column chromatography (e.g., ion exchange, affinity, gel exclusion, reversed-phase high pressure, fast protein liquid, etc.), differential centrifugation, differential solubility, or by

any other standard technique used for the purification of proteins. Functional properties may be evaluated using any suitable assay known in the art.

Alternatively, once a component protein or its derivative, is identified, the amino acid sequence of the protein can be deduced from the nucleic acid sequence of the chimeric gene from which it was encoded. As a result, the protein or its derivative can be synthesized by standard chemical methods known in the art (e.g., Hunkapiller et al., 1984, *Nature* 310:105-111).

Manipulations of component protein sequences may be made at the protein level. Included within the scope of the invention is a complex in which the component proteins or derivatives and analogs that are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease,  $\text{NaBH}_4$ , acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

In specific embodiments, the amino acid sequences are modified to include a fluorescent label. In another specific embodiment, the protein sequences are modified to have a heterofunctional reagent; such heterofunctional reagents can be used to crosslink the members of the complex.

In addition, complexes of analogs and derivatives of component proteins can be chemically synthesized. For example, a peptide corresponding to a portion of a component protein, which comprises the desired domain or mediates the desired activity in vitro (e.g., complex formation) can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the protein sequence.

In cases where natural products are suspected of being mutant or are isolated from new species, the amino acid sequence of a component protein isolated from the natural source, as well as those expressed in vitro, or from synthesized expression vectors in vivo or in vitro, can be determined from analysis of the DNA sequence, or alternatively, by direct sequencing of the isolated protein. Such analysis can be performed by manual sequencing or through use of an automated amino acid sequenator.

The complexes can also be analyzed by hydrophilicity analysis (Hopp and Woods, 1981, Proc. Natl. Acad. Sci. USA 78:3824-3828). A hydrophilicity profile can be used to identify the hydrophobic and hydrophilic regions of the proteins, and help predict their orientation in designing substrates for experimental manipulation, such as in binding experiments, antibody synthesis, etc. Secondary structural analysis can also be done to identify regions of the component proteins, or their derivatives, that assume specific structures (Chou and Fasman, 1974, Biochemistry 13:222-23). Manipulation, translation, secondary structure prediction, hydrophilicity and hydrophobicity profile predictions, open reading frame prediction and plotting, and determination of sequence homologies, etc., can be accomplished using computer software programs available in the art.

Other methods of structural analysis including but not limited to X-ray crystallography (Engstrom, 1974, Biochem. Exp. Biol. 11:7-13), mass spectroscopy and gas chromatography (Methods in Protein Science, J. Wiley and Sons, New York, 1997), and computer modeling (Fletterick and Zoller, eds., 1986, Computer Graphics and Molecular Modeling, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, New York) can also be employed.

#### 4.2 ANTIBODIES TO PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

According to the present invention, a protein complex of the present invention comprising a first protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, can be used as an immunogen to generate antibodies which immunospecifically bind such immunogen. According to the present invention, also a protein complex of the present invention can be used as an immunogen to generate antibodies which immunospecifically bind to such immunogen comprising all proteins listed in fifth column of table 1.

Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library. In a specific embodiment, antibodies to a complex comprising human protein components are

produced. In another embodiment, a complex formed from a fragment of said first protein and a fragment of said second protein, which fragments contain the protein domain that interacts with the other member of the complex, are used as an immunogen for antibody production. In a preferred embodiment, the antibody specific for the complex in that the antibody does not bind the individual protein components of the complex.

Polyclonal antibodies can be prepared as described above by immunizing a suitable subject with a polypeptide of the invention as an immunogen. Preferred polyclonal antibody compositions are ones that have been selected for antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred polyclonal antibody preparations are ones that contain only antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a polypeptide of the invention. In such a manner, the only human epitope or epitopes recognized by the resulting antibody compositions raised against this immunogen will be present as part of a polypeptide or polypeptides of the invention.

The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. If desired, the antibody molecules can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. Alternatively, antibodies specific for a protein or polypeptide of the invention can be selected for (e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, i.e., one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those on the desired protein or polypeptide of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at



most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein or polypeptide of the invention.

At an appropriate time after immunization, e.g., when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein, 1975, *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al., 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (Cole et al., 1985, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology* 1994, Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a polypeptide of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al., 1991, *Bio/Technology* 9:1370-1372; Hay et al., 1992, *Hum. Antibod. Hybridomas* 3:81-85; Huse et al., 1989, *Science* 246:1275-1281; Griffiths et al., 1993, *EMBO J.* 12:725-734.

Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. A chimeric antibody is a molecule in which different portions are derived from different



animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from non-human species having one or more complementarily determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al., 1988, *Science* 240:1041-1043; Liu et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al., 1987, *J. Immunol.* 139:3521-3526; Sun et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura et al., 1987, *Canc. Res.* 47:999-1005; Wood et al., 1985, *Nature* 314:446-449; and Shaw et al., 1988, *J. Natl. Cancer Inst.* 80:1553-1559; Morrison, 1985, *Science* 229:1202-1207; Oi et al., 1986, *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al., 1986, *Nature* 321:552-525; Verhoeyan et al., 1988, *Science* 239:1534; and Beidler et al., 1988, *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, 1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In

addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., 1994, *Bio/technology* 12:899-903).

Antibody fragments that contain the idiotypes of the complex can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')<sub>2</sub> fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments.

In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, e.g., ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of the complex, or a derivative thereof, one may assay generated hybridomas for a product that binds to the fragment of the complex, or a derivative thereof, that contains such a domain. For selection of an antibody that specifically binds a complex of the present, or a derivative, or homologue thereof, but which does not specifically bind to the individual proteins of the complex, or a derivative, or homologue thereof, one can select on the basis of positive binding to the complex and a lack of binding to the individual protein components.

Antibodies specific to a domain of the complex, or a derivative, or homologue thereof, are also provided.

The foregoing antibodies can be used in methods known in the art relating to the localization and/or quantification of the complexes of the invention, e.g., for imaging these proteins, measuring levels thereof in appropriate physiological samples (by immunoassay), in diagnostic methods, etc. This hold true also for a derivative, or homologue thereof of a complex.

In another embodiment of the invention (see *infra*), an antibody to a complex or a fragment of such antibodies containing the antibody binding domain, is a therapeutic.

#### 4.3 DIAGNOSTIC, PROGNOSTIC, AND SCREENING USES OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The particular protein complexes and proteins of the present invention may be markers of normal physiological processes, and thus have diagnostic utility. Further, definition of particular groups of patients with elevations or deficiencies of a protein complex of the present invention, or wherein the protein complex has a change in protein component composition, can lead to new nosological classifications of diseases, furthering diagnostic ability.

Examples for diseases or disorders are those as listed in table 4

Detecting levels of protein complexes, or individual component proteins that form the complexes, or detecting levels of the mRNAs encoding the components of the complex, may be used in diagnosis, prognosis, and/or staging to follow the course of a disease state, to follow a therapeutic response, etc.

A protein complex of the present invention and the individual components of the complex and a derivative, analog or subsequence thereof, encoding nucleic acids (and sequences complementary thereto), and anti-complex antibodies and antibodies directed against individual components that can form the complex, are useful in diagnostics. The foregoing molecules can be used in assays, such as immunoassays, to detect, prognose, diagnose, or monitor various conditions, diseases, and disorders characterized by aberrant levels of a complex or aberrant component composition of a complex, or monitor the treatment of such various conditions, diseases, and disorders.

In particular, such an immunoassay is carried out by a method comprising contacting a sample derived from a patient with an anti-complex antibody under conditions such that immunospecific binding can occur, and detecting or measuring the amount of any immunospecific binding by the antibody. In a specific aspect, such binding of antibody, in tissue sections, can be used to detect aberrant complex localization, or aberrant (e.g., high, low or absent) levels of a protein complex or complexes. In a specific embodiment, an antibody to the complex can be used to assay a patient tissue or serum sample for the presence of the complex, where an aberrant level of the complex is an indication of a diseased condition. By "aberrant levels" is meant increased or decreased levels relative to that present, or a standard level

representing that present, in an analogous sample from a portion or fluid of the body, or from a subject not having the disorder.

The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as Western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few known in the art.

Nucleic acids encoding the components of the protein complex and related nucleic acid sequences and subsequences, including complementary sequences, can be used in hybridization assays. The nucleic acid sequences, or subsequences thereof, comprising about at least 8 nucleotides, can be used as hybridization probes. Hybridization assays can be used to detect, prognose, diagnose, or monitor conditions, disorders, or disease states associated with aberrant levels of the mRNAs encoding the components of a complex as described, supra. In particular, such a hybridization assay is carried out by a method comprising contacting a sample containing nucleic acid with a nucleic acid probe capable of hybridizing to component protein coding DNA or RNA, under conditions such that hybridization can occur, and detecting or measuring any resulting hybridization.

In specific embodiments, diseases and disorders involving or characterized by aberrant levels of a protein complex or aberrant complex composition can be diagnosed, or its suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by determining the component protein composition of the complex, or detecting aberrant levels of a member of the complex or un-complexed component proteins or encoding nucleic acids, or functional activity including, but not restricted to, binding to an interacting partner, or by detecting mutations in component protein RNA, DNA or protein (e.g., mutations such as translocations, truncations, changes in nucleotide or amino acid sequence relative to wild-type that cause increased or decreased expression or activity of a complex, and/or component protein.

Such diseases and disorders include, but are not limited to neurodegenerative disease such as listed in table 4.

By way of example, levels of a protein complex and the individual components of a complex can be detected by immunoassay, levels of component protein RNA or DNA



can be detected by hybridization assays (e.g., Northern blots, dot blots, RNase protection assays), and binding of component proteins to each other (e.g., complex formation) can be measured by binding assays commonly known in the art. Translocations and point mutations in component protein genes can be detected by Southern blotting, RFLP analysis, PCR using primers that preferably generate a fragment spanning at least most of the gene by sequencing of genomic DNA or cDNA obtained from the patient, etc.

Assays well known in the art (e.g., assays described above such as immunoassays, nucleic acid hybridization assays, activity assays, etc.) can be used to determine whether one or more particular protein complexes are present at either increased or decreased levels, or are absent, in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the levels in samples from subjects not having such a disease or disorder, or having a predisposition to develop such a disease or disorder. Additionally, these assays can be used to determine whether the ratio of the complex to the un-complexed components of the complex, is increased or decreased in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the ratio in samples from subjects not having such a disease or disorder.

In the event that levels of one or more particular protein complexes (i.e., complexes formed from component protein derivatives, homologs, fragments, or analogs) are determined to be increased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder, or predisposition for a disease or disorder, can be diagnosed, have prognosis defined for, be screened for, or be monitored by detecting increased levels of the one or more protein complexes, increased levels of the mRNA that encodes one or more members of the one or more particular protein complexes, or by detecting increased complex functional activity.

Accordingly, in a specific embodiment of the present invention, diseases and disorders involving increased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting increased levels of the one or more protein complexes, the mRNA encoding both members of the complex, or complex functional activity, or by detecting mutations in the component proteins that stabilize or enhance



complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that stabilize or enhance complex formation.

In the event that levels of one or more particular protein complexes are determined to be decreased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder or predisposition for a disease or disorder can be diagnosed, have its prognosis determined, be screened for, or be monitored by detecting decreased levels of the one or more protein complexes, the mRNA that encodes one or more members of the particular one or more protein complexes, or by detecting decreased protein complex functional activity.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving decreased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting decreased levels of the one or more protein complexes, the mRNA encoding one or more members of the one or more complexes, or complex functional activity, or by detecting mutations in the component proteins that decrease complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that decrease complex formation.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving aberrant compositions of the complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting the component proteins of one or more complexes, or the mRNA encoding the members of the one or more complexes.

The use of detection techniques, especially those involving antibodies against a protein complex, provides a method of detecting specific cells that express the complex or component proteins. Using such assays, specific cell types can be defined in which one or more particular protein complexes are expressed, and the presence of the complex or component proteins can be correlated with cell viability, state, health, etc.

Also embodied are methods to detect a protein complex of the present invention in cell culture models that express particular protein complexes or derivatives thereof, for the purpose of characterizing or preparing the complexes for harvest. This embodiment includes cell sorting of prokaryotes such as but not restricted to bacteria (Davey and Kell,

1996, Microbiol. Rev. 60:641-696), primary cultures and tissue specimens from eukaryotes, including mammalian species such as human (Steele et al., 1996, Clin. Obstet. Gynecol 39:801-813), and continuous cell cultures (Orfao and Ruiz-Arguelles, 1996, Clin. Biochem. 29:5-9). Such isolations can be used as methods of diagnosis, described, supra.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

#### 4.4 THERAPEUTIC USES OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The present invention is directed to a method for treatment or prevention of various diseases and disorders by administration of a therapeutic compound (termed herein "therapeutic"). Such "therapeutics" include, but are not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments) of the foregoing (e.g., as described hereinabove); antibodies thereto (as described hereinabove); nucleic acids encoding the component protein, and analogs or derivatives, thereof (e.g., as described hereinabove); component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The protein complexes as identified herein can be implicated in processes which are implicated in or associated with pathological conditions.

Diseases and disorders which can be treated and/or prevented and/or diagnosed by therapeutics interacting with any of the complexes provided herein are for example those listed in table 4.

These disorders are treated or prevented by administration of a therapeutic that modulates (i.e. inhibits or promotes) protein complex activity or formation or modulates its function or composition. Diseases or disorders associated with aberrant levels of complex activity or formation, or aberrant levels or activity of the component proteins, or aberrant complex composition or a change in the function, may be treated by administration of a therapeutic that modulates complex formation or activity or by the administration of a protein complex.

Therapeutics may also be administered to modulate complex formation or activity or level thereof in a microbial organism such as yeast, fungi such as candida albicans causing an infectious disease in animals or humans.

Diseases and disorders characterized by increased (relative to a subject not suffering from the disease or disorder) complex levels or activity can be treated with therapeutics that antagonize (i.e., reduce or inhibit) complex formation or activity. Therapeutics that can be used include, but are not limited to, the component proteins or an analog, derivative or fragment of the component protein; anti-complex antibodies (e.g., antibodies specific for the protein complex, or a fragment or derivative of the

antibody containing the binding region thereof; nucleic acids encoding the component proteins; antisense nucleic acids complementary to nucleic acids encoding the component proteins; and nucleic acids encoding the component protein that are dysfunctional due to, e.g., a heterologous insertion within the protein coding sequence, that are used to "knockout" endogenous protein function by homologous recombination, see, e.g., Capecchi, 1989, *Science* 244:1288-1292. In one embodiment, a therapeutic is 1, 2 or more antisense nucleic acids which are complementary to 1, 2, or more nucleic acids, respectfully, that encode component proteins of a complex.

In a specific embodiment of the present invention, a nucleic acid containing a portion of a component protein gene in which gene sequences flank (are both 5' and 3' to) a different gene sequence, is used as a component protein antagonist, or to promote component protein inactivation by homologous recombination (see also, Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342: 435-438). Additionally, mutants or derivatives of a component protein that has greater affinity for another component protein or the complex than wild type may be administered to compete with wild type protein for binding, thereby reducing the levels of complexes containing the wild type protein. Other therapeutics that inhibit complex function can be identified by use of known convenient in vitro assays, e.g., based on their ability to inhibit complex formation, or as described in Section 4.5, *infra*.

In specific embodiments, therapeutics that antagonize complex formation or activity are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an increased (relative to normal or desired) level of a complex, for example, in patients where complexes are overactive or overexpressed; or (2) in diseases or disorders where an in vitro (or in vivo) assay (see *infra*) indicates the utility of antagonist administration. Increased levels of a complex can be readily detected, e.g., by quantifying protein and/or RNA, by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, or structure and/or activity of the expressed complex (or the encoding mRNA). Many methods standard in the art can be thus employed including, but not limited to, immunoassays to detect complexes and/or visualize complexes (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.), and/or hybridization assays to detect concurrent expression of component protein mRNA (e.g., Northern assays, dot blot analysis, in situ hybridization, etc.).



A more specific embodiment of the present invention is directed to a method of reducing complex expression (i.e., expression of the protein components of the complex and/or formation of the complex) by targeting mRNAs that express the protein moieties. RNA therapeutics currently fall within three classes, antisense species, ribozymes, or RNA aptamers (Good et al., 1997, *Gene Therapy* 4:45-54).

Antisense oligonucleotides have been the most widely used. By way of example, but not limitation, antisense oligonucleotide methodology to reduce complex formation is presented below, *infra*. Ribozyme therapy involves the administration, induced expression, etc. of small RNA molecules with enzymatic ability to cleave, bind, or otherwise inactivate specific RNAs, to reduce or eliminate expression of particular proteins (Grassi and Marini, 1996, *Annals of Medicine* 28:499-510; Gibson, 1996, *Cancer and Metastasis Reviews* 15:287-299). RNA aptamers are specific RNA ligand proteins, such as for Tat and Rev RNA (Good et al., 1997, *Gene Therapy* 4:45-54) that can specifically inhibit their translation. Aptamers specific for component proteins can be identified by many methods well known in the art, for example, by affecting the formation of a complex in the protein-protein interaction assay described, *infra*.

In another embodiment, the activity or levels of a component protein are reduced by administration of another component protein, or the encoding nucleic acid, or an antibody that immunospecifically binds to the component protein, or a fragment or a derivative of the antibody containing the binding domain thereof.

In another aspect of the invention, diseases or disorders associated with increased levels of an component protein of the complex may be treated or prevented by administration of a therapeutic that increases complex formation if the complex formation acts to reduce or inactivate the component protein through complex formation. Such diseases or disorders can be treated or prevented by administration of one component member of the complex, administration of antibodies or other molecules that stabilize the complex, etc.

Diseases and disorders associated with underexpression of a complex, or a component protein, are treated or prevented by administration of a therapeutic that promotes (i.e., increases or supplies) complex levels and/or function, or individual component protein function. Examples of such a therapeutic include but are not limited to a complex or a derivative, analog or fragment of the complex that are functionally active (e.g., able to form a complex), un-complexed component proteins and derivatives, analogs, and fragments of un-complexed component proteins, and nucleic acids



encoding the members of a complex or functionally active derivatives or fragments of the members of the complex, e.g., for use in gene therapy. In a specific embodiment, a therapeutic includes derivatives, homologs or fragments of a component protein that increase and/or stabilize complex formation. Examples of other agonists can be identified using in vitro assays or animal models, examples of which are described, *infra*.

In yet other specific embodiments of the present invention, therapeutics that promote complex function are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an absence or decreased (relative to normal or desired) level of a complex, for example, in patients where a complex, or the individual components necessary to form the complex, is lacking, genetically defective, biologically inactive or underactive, or under-expressed; or (2) in diseases or disorders wherein an in vitro or in vivo assay (see, *infra*) indicates the utility of complex agonist administration. The absence or decreased level of a complex, component protein or function can be readily detected, e.g., by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, structure and/or activity of the expressed complex and/or the concurrent expression of mRNA encoding the two components of the complex. Many methods standard in the art can be thus employed, including but not limited to immunoassays to detect and/or visualize a complex, or the individual components of a complex (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs encoding the individual protein components of a complex by detecting and/or visualizing component mRNA concurrently or separately using, e.g., Northern assays, dot blot analysis, in situ hybridization, etc.

In specific embodiments, the activity or levels of a component protein are increased by administration of another component protein of the same complex, or a derivative, homolog or analog thereof, a nucleic acid encoding the other component, or an agent that stabilizes or enhances the other component, or a fragment or derivative of such an agent.

Generally, administration of products of species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, a human complex, or derivative, homolog or analog thereof; nucleic acids encoding the members of the human complex or a derivative, homolog or analog thereof; an antibody to a human complex, or a derivative thereof; or other human

agents that affect component proteins or the complex, are therapeutically or prophylactically administered to a human patient.

Preferably, suitable in vitro or in vivo assays are utilized to determine the effect of a specific therapeutic and whether its administration is indicated for treatment of the affected tissue or individual.

In various specific embodiments, in vitro assays can be carried out with representative cells of cell types involved in a patient's disorder, to determine if a therapeutic has a desired effect upon such cell types.

Compounds for use in therapy can be tested in suitable animal model systems prior to testing in humans, including, but not limited to, rats, mice, chicken, cows, monkeys, rabbits, etc. For in vivo testing, prior to administration to humans, any animal model system known in the art may be used. Additional descriptions and sources of therapeutics that can be used according to the invention are found in Sections 4.1 to 4.3 and 4.7 herein.

#### 4.4.1 GENE THERAPY

In a specific embodiment of the present invention, nucleic acids comprising a sequence encoding the component proteins, or a functional derivative thereof, are administered to modulate complex activity or formation by way of gene therapy. Gene therapy refers to therapy performed by the administration of a nucleic acid to a subject. In this embodiment of the present invention, the nucleic acid expresses its encoded protein(s) that mediates a therapeutic effect by modulating complex activity or formation. Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, *Clinical Pharmacy* 12:488-505; Wu and Wu, 1991, *Biotherapy* 3:87-95; Tolstoshev, 1993, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596; Mulligan, 1993, *Science* 260:926-932; Morgan and Anderson, 1993, *Ann. Rev. Biochem.* 62:191-217; and May, 1993, *TIBTECH* 11:155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al., eds., 1993, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY; and Kriegler, 1990, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY.

In a preferred aspect, the therapeutic comprises a nucleic acid that is part of an expression vector that expresses one or more of the component proteins, or fragments or chimeric proteins thereof, in a suitable host. In particular, such a nucleic acid has a promoter operably linked to the protein coding region(s) (or, less preferably separate promoters linked to the separate coding regions separately), said promoter being inducible or constitutive, and optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule is used in which the coding sequences, and any other desired sequences, are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intra-chromosomal expression of the component protein nucleic acids (Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342:435-438).

Delivery of the nucleic acid into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vector, or indirect, in which case, cells are first transformed with the nucleic acid in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid is directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by infection using a defective or attenuated retroviral or other viral vector (U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors, or through use of transfecting agents, by encapsulation in liposomes, microparticles, or microcapsules, or by administering it in linkage to a peptide that is known to enter the nucleus, or by administering it in linkage to a ligand subject to receptor-mediated endocytosis that can be used to target cell types specifically expressing the receptors (e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432), etc. In another embodiment, a nucleic acid-ligand complex can be formed in which the ligand comprises a fusogenic viral peptide that disrupts endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., International Patent Publications WO 92/06180; WO 92/22635; WO 92/20316; WO 93/14188; and WO 93/20221. Alternatively, the nucleic acid can be introduced

intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342:435-438).

In a specific embodiment, a viral vector that contains the component protein encoding nucleic acids is used. For example, a retroviral vector can be used (Miller et al., 1993, *Meth. Enzymol.* 217:581-599). These retroviral vectors have been modified to delete retroviral sequences that are not necessary for packaging of the viral genome and integration into host cell DNA. The encoding nucleic acids to be used in gene therapy is/are cloned into the vector, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., 1994, *Biotherapy* 6:291-302, which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are Clowes et al., 1994, *J. Clin. Invest.* 93:644-651; Kiem et al., 1994, *Blood* 83:1467-1473; Salmons and Gunzberg, 1993, *Human Gene Therapy* 4:129-141; and Grossman and Wilson, 1993, *Curr. Opin. in Genetics and Devel.* 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are the liver, the central nervous system, endothelial cells and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, *Curr. Opin. Genet. Devel.* 3:499-503, discuss adenovirus-based gene therapy. The use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys has been demonstrated by Bout et al., 1994, *Human Gene Therapy* 5:3-10. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, *Science* 252:431-434; Rosenfeld et al., 1992, *Cell* 68:143-155; and Mastrangeli et al., 1993, *J. Clin. Invest.* 91:225-234.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, *Proc. Soc. Exp. Biol. Med.* 204:289-300).

Another approach to gene therapy involves transferring a gene into cells in tissue culture by methods such as electroporation, lipofection, calcium phosphate-mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those



cells that have taken up and are expressing the transferred gene from these that have not. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art including, but not limited to, transfection by electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, 1993, *Meth. Enzymol.* 217:599-618; Cohen et al., 1993, *Meth. Enzymol.* 217:618-644; Cline, 1985, *Pharmac. Ther.* 29:69-92) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably, is heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. In a preferred embodiment, epithelial cells are injected, e.g., subcutaneously. In another embodiment, recombinant skin cells may be applied as a skin graft onto the patient. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes, blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, and granulocytes, various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, a component protein encoding nucleic acid is/are introduced into the cells such that the gene or genes are expressible by the cells or their progeny, and the recombinant cells

are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention. Such stem cells include but are not limited to hematopoietic stem cells (HSCs), stem cells of epithelial tissues such as the skin and the lining of the gut, embryonic heart muscle cells, liver stem cells (International Patent Publication WO 94/08598), and neural stem cells (Stemple and Anderson, 1992, Cell 71:973-985).

Epithelial stem cells (ESCs), or keratinocytes, can be obtained from tissues such as the skin and the lining of the gut by known procedures (Rheinwald, 1980, Meth. Cell Biol. 2A:229). In stratified epithelial tissue such as the skin, renewal occurs by mitosis of stem cells within the germinal layer, the layer closest to the basal lamina. Similarly, stem cells within the lining of the gut provide for a rapid renewal rate of this tissue. ESCs or keratinocytes obtained from the skin or lining of the gut of a patient or donor can be grown in tissue culture (Rheinwald, 1980, Meth. Cell Bio. 2A:229; Pittelkow and Scott, 1986, Mayo Clinic Proc. 61:771). If the ESCs are provided by a donor, a method for suppression of host versus graft reactivity (e.g., irradiation, or drug or antibody administration to promote moderate immunosuppression) can also be used.

With respect to hematopoietic stem cells (HSCs), any technique that provides for the isolation, propagation, and maintenance in vitro of HSCs can be used in this embodiment of the invention. Techniques by which this may be accomplished include (a) the isolation and establishment of HSC cultures from bone marrow cells isolated from the future host, or a donor, or (b) the use of previously established long-term HSC cultures, which may be allogeneic or xenogeneic. Non-autologous HSCs are used preferably in conjunction with a method of suppressing transplantation immune reactions between the future host and patient. In a particular embodiment of the present invention, human bone marrow cells can be obtained from the posterior iliac crest by needle aspiration (see, e.g., Kodo et al., 1984, J. Clin. Invest. 73: 1377-1384). In a preferred embodiment of the present invention, the HSCs can be made highly enriched or in substantially pure form. This enrichment can be accomplished before, during, or after long-term culturing, and can be done by any technique known in the art. Long-term cultures of bone marrow cells can be established and maintained by using, for example, modified Dexter cell culture techniques (Dexter et al., 1977, J. Cell Physiol. 91:335) or Witlock-Witte culture techniques (Witlock and Witte, 1982, Proc. Natl. Acad. Sci. USA 79:3608-3612).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Additional methods can be adapted for use to deliver a nucleic acid encoding the component proteins, or functional derivatives thereof, e.g., as described in Section 4.1, *supra*.

#### 4.4.2 USE OF ANTISENSE OLIGONUCLEOTIDES FOR SUPPRESSION OF PROTEIN COMPLEX FORMATION OR PROTEIN COMPLEX/PROTEIN ACTIVITY

In a specific embodiment of the present invention, protein complex activity and formation and protein activity is inhibited by use of antisense nucleic acids for the component proteins of the complex, that inhibit transcription and/or translation of their complementary sequence. The present invention provides the therapeutic or prophylactic use of nucleic acids of at least six nucleotides that are antisense to a gene or cDNA encoding a component protein, or a portion thereof. An "antisense" nucleic acid as used herein refers to a nucleic acid capable of hybridizing to a sequence-specific portion of a component protein RNA (preferably mRNA) by virtue of some sequence complementarity. The antisense nucleic acid may be complementary to a coding and/or noncoding region of a component protein mRNA. Such antisense nucleic acids that inhibit complex formation or activity have utility as therapeutics, and can be used in the treatment or prevention of disorders as described *supra*.

The antisense nucleic acids of the invention can be oligonucleotides that are double-stranded or single-stranded, RNA or DNA, or a modification or derivative thereof, which can be directly administered to a cell, or which can be produced intracellularly by transcription of exogenous, introduced sequences.

In another embodiment, the present invention is directed to a method for inhibiting the expression of component protein nucleic acid sequences, in a prokaryotic or eukaryotic cell, comprising providing the cell with an effective amount of a composition comprising an antisense nucleic acid of the component protein, or a derivative thereof, of the invention.

The antisense nucleic acids are of at least six nucleotides and are preferably oligonucleotides, ranging from 6 to about 200 nucleotides. In specific aspects, the oligonucleotide is at least 10 nucleotides, at least 15 nucleotides, at least 100 nucleotides, or at least 200 nucleotides. The oligonucleotides can be DNA or RNA or chimeric mixtures, or derivatives or modified versions thereof, and either single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:648-652; International Patent Publication No. WO 88/09810) or blood-brain barrier (see, e.g., International Patent Publication No. WO 89/10134), hybridization-triggered cleavage agents (see, e.g., Krol et al., 1988, *BioTechniques* 6:958-976), or intercalating agents (see, e.g., Zon, 1988, *Pharm. Res.* 5:539-549).

In a preferred aspect of the invention, an antisense oligonucleotide is provided, preferably as single-stranded DNA. The oligonucleotide may be modified at any position in its structure with constituents generally known in the art.

The antisense oligonucleotides may comprise at least one modified base moiety which is selected from the group including but not limited to 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl)uracil, 5-carboxymethylaminomethyl-2-thio-uridine, 5-carboxymethylaminomethyluracil, dihydrouracil,  $\beta$ -D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil,  $\beta$ -D-mannosylqueosine, 5N-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methyl-thio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

In another embodiment, the oligonucleotide comprises at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.



In yet another embodiment, the oligonucleotide comprises at least one modified phosphate backbone selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal, or an analog of the foregoing.

In yet another embodiment, the oligonucleotide is a 2'-a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641).

The oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

Oligonucleotides of the invention may be synthesized by standard methods known in the art, e.g., by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligo-nucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. USA 85:7448-7451), etc.

In a specific embodiment, the antisense oligonucleotides comprise catalytic RNAs, or ribozymes (see, e.g., International Patent Publication No. WO 90/11364; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2'-O-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In an alternative embodiment, the antisense nucleic acids of the invention are produced intracellularly by transcription from an exogenous sequence. For example, a vector can be introduced in vivo such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the component protein. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art to be capable of replication and expression in

mammalian cells. Expression of the sequences encoding the antisense RNAs can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., 1980, Cell 22:787-797), the herpes thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. USA 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a component protein gene, preferably a human gene. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with a component protein RNA it may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The component protein antisense nucleic acids can be used to treat (or prevent) disorders of a cell type that expresses, or preferably overexpresses, a protein complex.

Cell types that express or overexpress component protein RNA can be identified by various methods known in the art. Such methods include, but are not limited to, hybridization with component protein-specific nucleic acids (e.g., by Northern blot hybridization, dot blot hybridization, or in situ hybridization), or by observing the ability of RNA from the cell type to be translated in vitro into the component protein by immunohistochemistry, Western blot analysis, ELISA, etc. In a preferred aspect, primary tissue from a patient can be assayed for protein expression prior to treatment, e.g., by immunocytochemistry, in situ hybridization, or any number of methods to detect protein or mRNA expression.

Pharmaceutical compositions of the invention (see Section 4.7, *infra*), comprising an effective amount of a protein component antisense nucleic acid in a pharmaceutically

acceptable carrier can be administered to a patient having a disease or disorder that is of a type that expresses or overexpresses a protein complex of the present invention.

The amount of antisense nucleic acid that will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. Where possible, it is desirable to determine the antisense cytotoxicity in vitro, and then in useful animal model systems, prior to testing and use in humans.

In a specific embodiment, pharmaceutical compositions comprising antisense nucleic acids are administered via liposomes, microparticles, or microcapsules. In various embodiments of the invention, it may be useful to use such compositions to achieve sustained release of the antisense nucleic acids. In a specific embodiment, it may be desirable to utilize liposomes targeted via antibodies to specific identifiable central nervous system cell types (Leonetti et al., 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2448-2451; Renneisen et al., 1990, J. Biol. Chem. 265:16337-16342).

#### 4.5 ASSAYS OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION AND DERIVATIVES AND ANALOGS THEREOF

The functional activity of a protein complex of the present invention, or a derivative, fragment or analog thereof or protein component thereof, can be assayed by various methods. Potential modulators (e.g., agonists and antagonists) of complex activity or formation, e.g., anti-complex antibodies and antisense nucleic acids, can be assayed for the ability to modulate complex activity or formation.

In one embodiment of the present invention, where one is assaying for the ability to bind or compete with a wild-type complex for binding to an anti-complex antibody, various immunoassays known in the art can be used, including but not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassay, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitin reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels), western blot analysis, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, etc. In

one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

The expression of the component protein genes (both endogenous and those expressed from cloned DNA containing the genes) can be detected using techniques known in the art, including but not limited to Southern hybridization (Southern, 1975, J. Mol. Biol. 98:503-517), northern hybridization (see, e.g., Freeman et al., 1983, Proc. Natl. Acad. Sci. USA 80:4094-4098), restriction endonuclease mapping (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2<sup>nd</sup> Ed. Cold Spring Harbor Laboratory Press, New York), RNase protection assays (Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1997), DNA sequence analysis, and polymerase chain reaction amplification (PCR; U.S. Patent Nos. 4,683,202, 4,683,195, and 4,889,818; Gyllenstein et al., 1988, Proc. Natl. Acad. Sci. USA 85:7652-7657; Ochman et al., 1988, Genetics 120:621-623; Loh et al., 1989, Science 243:217-220) followed by Southern hybridization with probes specific for the component protein genes, in various cell types. Methods of amplification other than PCR commonly known in the art can be employed. In one embodiment, Southern hybridization can be used to detect genetic linkage of component protein gene mutations to physiological or pathological states. Various cell types, at various stages of development, can be characterized for their expression of component proteins at the same time and in the same cells. The stringency of the hybridization conditions for northern or Southern blot analysis can be manipulated to ensure detection of nucleic acids with the desired degree of relatedness to the specific probes used. Modifications to these methods and other methods commonly known in the art can be used.

Derivatives (e.g., fragments), homologs and analogs of one component protein can be assayed for binding to another component protein in the same complex by any method known in the art, for example the modified yeast matrix mating test described in Section 4.6.1 *infra*, immunoprecipitation with an antibody that binds to the component protein complexed with other component proteins in the same complex, followed by size fractionation of the immunoprecipitated proteins (e.g., by denaturing or nondenaturing polyacrylamide gel electrophoresis), Western blot analysis, etc.



One embodiment of the invention provides a method for screening a derivative, homolog or analog of a component protein for biological activity comprising contacting said derivative, homolog or analog of the component protein with the other component proteins in the same complex; and detecting the formation of a complex between said derivative, homolog or analog of the component protein and the other component proteins; wherein detecting formation of said complex indicates that said derivative, homolog or analog of has biological (e.g., binding) activity.

The invention also provides methods of modulating the activity of a component protein that can participate in a protein complex by administration of a binding partner of that protein or derivative, homolog or analog thereof.

In a specific embodiment of the present invention, a protein complex of the present invention is administered to treat or prevent a disease or disorder, since the complex and/or component proteins have been implicated in the disease and disorder. Accordingly, a protein complex or a derivative, homolog, analog or fragment thereof, nucleic acids encoding the component proteins, anti-complex antibodies, and other modulators of protein complex activity, can be tested for activity in treating or preventing a disease or disorder in in vitro and in vivo assays.

In one embodiment, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by contacting cultured cells that exhibit an indicator of the disease in vitro, with the therapeutic, and comparing the level of said indicator in the cells contacted with the therapeutic, with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the therapeutic has activity in treating or preventing the disease.

In another embodiment of the invention, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by administering the therapeutic to a test animal that is predisposed to develop symptoms of a disease, and measuring the change in said symptoms of the disease after administration of said therapeutic, wherein a reduction in the severity of the symptoms of the disease or prevention of the symptoms of the disease indicates that the therapeutic has activity in treating or preventing the disease. Such a test animal can be any one of a number of animal models known in the art for disease. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention.

#### 4.6 SCREENING FOR MODULATORS OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

A complex of the present invention, the component proteins of the complex and nucleic acids encoding the component proteins, as well as derivatives and fragments of the amino and nucleic acids, can be used to screen for compounds that bind to, or modulate the amount of, activity of, or protein component composition of, said complex, and thus, have potential use as modulators, i.e., agonists or antagonists, of complex activity, and/or complex formation, i.e., the amount of complex formed, and/or protein component composition of the complex.

Thus, the present invention is also directed to methods for screening for molecules that bind to, or modulate the function of, amount of, activity of, formation of or protein component composition of, a complex of the present invention. In one embodiment of the invention, the method for screening for a molecule that modulates directly or indirectly the function, activity or formation of a complex of the present invention comprises exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules under conditions conducive to modulation; and determining the amount of, the biochemical activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a protein or protein complex dependend on the function of the complex and/or product of a gene dependend on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a protein or protein complex dependend on the function of the complex and/or product of a gene dependend on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

In another embodiment, the present invention further relates to a process for the identification and/or preparation of an effector of the complex comprising the step of bringing into contact a product of any of claims 1 to 8 with a compound, a mixture or a library of compounds and determining whether the compound or a certain compound of the mixture or library binds to the product and/or effects the products biological activity and optionally further purifying the compound positively tested as effector.

In another embodiment, the present invention is directed to a method for screening for a molecule that binds a protein complex of the present invention comprising exposing said complex, or a cell or organism containing the complex

machinery, to one or more candidate molecules; and determining whether said complex is bound by any of said candidate molecules. Such screening assays can be carried out using cell-free and cell-based methods that are commonly known in the art in vitro, in vivo or ex vivo. For example, an isolated complex can be employed, or a cell can be contacted with the candidate molecule and the complex can be isolated from such contacted cells and the isolated complex can be assayed for activity or component composition. In another example, a cell containing the complex can be contacted with the candidate molecule and the levels of the complex in the contacted cell can be measured. Additionally, such assays can be carried out in cells recombinantly expressing a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a component protein from fifth column of table 1, or a functionally active fragment or functionally active derivative thereof. Additionally, such assays can also be carried out in cells recombinantly expressing all component proteins from the group of proteins in the fifth column of table 1.

For example, assays can be carried out using recombinant cells expressing the protein components of a complex, to screen for molecules that bind to, or interfere with, or promote complex activity or formation. In preferred embodiments, polypeptide derivatives that have superior stabilities but retain the ability to form a complex (e.g., one or more component proteins modified to be resistant to proteolytic degradation in the binding assay buffers, or to be resistant to oxidative degradation), are used to screen for modulators of complex activity or formation. Such resistant molecules can be generated, e.g., by substitution of amino acids at proteolytic cleavage sites, the use of chemically derivatized amino acids at proteolytic susceptible sites, and the replacement of amino acid residues subject to oxidation, i.e. methionine and cysteine.

A particular aspect of the present invention relates to identifying molecules that inhibit or promote formation or degradation of a complex of the present invention, e.g., using the method described for isolating the complex and identifying members of the complex using the TAP assay described in Section 4, *infra*, and in WO 00/09716 and Rigaut et al., 1999, *Nature Biotechnol.* 17:1030-1032, which are each incorporated by reference in their entirety. TNRF1

In another embodiment of the invention, a modulator is identified by administering a candidate molecule to a transgenic non-human animal expressing the complex component proteins from promoters that are not the native promoters of the respective



proteins, more preferably where the candidate molecule is also recombinantly expressed in the transgenic non-human animal. Alternatively, the method for identifying such a modulator can be carried out in vitro, preferably with a purified complex, and a purified candidate molecule.

Agents/molecules (candidate molecules) to be screened can be provided as mixtures of a limited number of specified compounds, or as compound libraries, peptide libraries and the like. Agents/molecules to be screened may also include all forms of antisera, antisense nucleic acids, etc., that can modulate complex activity or formation. Exemplary candidate molecules and libraries for screening are set forth in Section 4.6.1, *infra*.

Screening the libraries can be accomplished by any of a variety of commonly known methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, *Adv. Exp. Med. Biol.* 251:215-218; Scott and Smith, 1990, *Science* 249:386-390; Fowlkes et al., 1992, *BioTechniques* 13:422-427; Oldenburg et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:5393-5397; Yu et al., 1994, *Cell* 76:933-945; Staudt et al., 1988, *Science* 241:577-580; Bock et al., 1992, *Nature* 355:564-566; Tuerk et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:6988-6992; Ellington et al., 1992, *Nature* 355:850-852; U.S. Patent No. 5,096,815, U.S. Patent No. 5,223,409, and U.S. Patent No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, *Science* 263:671-673; and International Patent Publication No. WO 94/18318.

In a specific embodiment, screening can be carried out by contacting the library members with a complex immobilized on a solid phase, and harvesting those library members that bind to the protein (or encoding nucleic acid or derivative). Examples of such screening methods, termed "panning" techniques, are described by way of example in Parmley and Smith, 1988, *Gene* 73:305-318; Fowlkes et al., 1992, *BioTechniques* 13:422-427; International Patent Publication No. WO 94/18318; and in references cited hereinabove.

In a specific embodiment, fragments and/or analogs of protein components of a complex, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex formation (amount of complex or composition of complex) or activity in the cell, which thereby inhibit complex activity or formation in the cell.

In one embodiment, agents that modulate (i.e., antagonize or agonize) complex activity or formation can be screened for using a binding inhibition assay, wherein agents

are screened for their ability to modulate formation of a complex under aqueous, or physiological, binding conditions in which complex formation occurs in the absence of the agent to be tested. Agents that interfere with the formation of complexes of the invention are identified as antagonists of complex formation. Agents that promote the formation of complexes are identified as agonists of complex formation. Agents that completely block the formation of complexes are identified as inhibitors of complex formation.

Methods for screening may involve labeling the component proteins of the complex with radioligands (e.g.,  $^{125}\text{I}$  or  $^3\text{H}$ ), magnetic ligands (e.g., paramagnetic beads covalently attached to photobiotin acetate), fluorescent ligands (e.g., fluorescein or rhodamine), or enzyme ligands (e.g., luciferase or  $\beta$ -galactosidase). The reactants that bind in solution can then be isolated by one of many techniques known in the art, including but not restricted to, co-immunoprecipitation of the labeled complex moiety using antisera against the unlabeled binding partner (or labeled binding partner with a distinguishable marker from that used on the second labeled complex moiety), immunoaffinity chromatography, size exclusion chromatography, and gradient density centrifugation. In a preferred embodiment, the labeled binding partner is a small fragment or peptidomimetic that is not retained by a commercially available filter. Upon binding, the labeled species is then unable to pass through the filter, providing for a simple assay of complex formation.

Methods commonly known in the art are used to label at least one of the component members of the complex. Suitable labeling methods include, but are not limited to, radiolabeling by incorporation of radiolabeled amino acids, e.g.,  $^3\text{H}$ -leucine or  $^{35}\text{S}$ -methionine, radiolabeling by post-translational iodination with  $^{125}\text{I}$  or  $^{131}\text{I}$  using the chloramine T method, Bolton-Hunter reagents, etc., or labeling with  $^{32}\text{P}$  using phosphorylase and inorganic radiolabeled phosphorous, biotin labeling with photobiotin-acetate and sunlamp exposure, etc. In cases where one of the members of the complex is immobilized, e.g., as described *infra*, the free species is labeled. Where neither of the interacting species is immobilized, each can be labeled with a distinguishable marker such that isolation of both moieties can be followed to provide for more accurate quantification, and to distinguish the formation of homomeric from heteromeric complexes. Methods that utilize accessory proteins that bind to one of the modified interactants to improve the sensitivity of detection, increase the stability of the complex, etc., are provided.

Typical binding conditions are, for example, but not by way of limitation, in an aqueous salt solution of 10-250 mM NaCl, 5-50 mM Tris-HCl, pH 5-8, and 0.5% Triton X-100 or other detergent that improves specificity of interaction. Metal chelators and/or divalent cations may be added to improve binding and/or reduce proteolysis. Reaction temperatures may include 4, 10, 15, 22, 25, 35, or 42 degrees Celsius, and time of incubation is typically at least 15 seconds, but longer times are preferred to allow binding equilibrium to occur. Particular complexes can be assayed using routine protein binding assays to determine optimal binding conditions for reproducible binding.

The physical parameters of complex formation can be analyzed by quantification of complex formation using assay methods specific for the label used, e.g., liquid scintillation counting for radioactivity detection, enzyme activity for enzyme-labeled moieties, etc. The reaction results are then analyzed utilizing Scatchard analysis, Hill analysis, and other methods commonly known in the arts (see, e.g., *Proteins, Structures, and Molecular Principles*, 2<sup>nd</sup> Edition (1993) Creighton, Ed., W.H. Freeman and Company, New York).

In a second common approach to binding assays, one of the binding species is immobilized on a filter, in a microtiter plate well, in a test tube, to a chromatography matrix, etc., either covalently or non-covalently. Proteins can be covalently immobilized using any method well known in the art, for example, but not limited to the method of Kadonaga and Tjian, 1986, *Proc. Natl. Acad. Sci. USA* 83:5889-5893, i.e., linkage to a cyanogen-bromide derivatized substrate such as CNBr-Sepharose 4B (Pharmacia). Where needed, the use of spacers can reduce steric hindrance by the substrate. Non-covalent attachment of proteins to a substrate include, but are not limited to, attachment of a protein to a charged surface, binding with specific antibodies, binding to a third unrelated interacting protein, etc.

Assays of agents (including cell extracts or a library pool) for competition for binding of one member of a complex (or derivatives thereof) with another member of the complex labeled by any means (e.g., those means described above) are provided to screen for competitors or enhancers of complex formation.

In specific embodiments, blocking agents to inhibit non-specific binding of reagents to other protein components, or absorptive losses of reagents to plastics, immobilization matrices, etc., are included in the assay mixture. Blocking agents include, but are not restricted to bovine serum albumin,  $\beta$ -casein, nonfat dried milk, Denhardt's reagent, Ficoll, polyvinylpyrrolidone, nonionic detergents (NP40, Triton X-100, Tween 20,

Tween 80, etc.), ionic detergents (e.g., SDS, LDS, etc.), polyethylene glycol, etc. Appropriate blocking agent concentrations allow complex formation.

After binding is performed, unbound, labeled protein is removed in the supernatant, and the immobilized protein retaining any bound, labeled protein is washed extensively. The amount of bound label is then quantified using standard methods in the art to detect the label as described, *supra*.

In another specific embodiments screening for modulators of the protein complexes/protein as provided herein can be carried out by attaching those and/or the antibodies as provided herein to a solid carrier. In a further specific embodiment, the invention relates to an array of said molecules.

The preparation of such an array containing different types of proteins, including antibodies) is well known in the art and is apparent to a person skilled in the art (see e.g. Ekins et al., 1989, *J. Pharm. Biomed. Anal.* 7:155-168; Mitchell et al. 2002, *Nature Biotechnol.* 20:225-229; Petricoin et al., 2002, *Lancet* 359:572-577; Templin et al., 2001, *Trends Biotechnol.* 20:160-166; Wilson and Nock, 2001, *Curr. Opin. Chem. Biol.* 6:81-85; Lee et al., 2002 *Science* 295:1702-1705; MacBeath and Schreiber, 2000, *Science* 289:1760; Blawas and Reichert, 1998, *Biomaterials* 19:595; Kane et al., 1999, *Biomaterials* 20:2363; Chen et al., 1997, *Science* 276:1425; Vaughan et al., 1996, *Nature Biotechnol.* 14:309-314; Mahler et al., 1997, *Immunotechnology* 3:31-43; Roberts et al., 1999, *Curr. Opin. Chem. Biol.* 3:268-273; Nord et al., 1997, *Nature Biotechnol.* 15:772-777; Nord et al., 2001, *Eur. J. Biochem.* 268:4269-4277; Brody and Gold, 2000, *Rev. Mol. Biotechnol.* 74:5-13; Karlstroem and Nygren, 2001, *Anal. Biochem.* 295:22-30; Nelson et al., 2000, *Electrophoresis* 21:1155-1163; Honore et al., 2001, *Expert Rev. Mol. Diagn.* 3:265-274; Albala, 2001, *Expert Rev. Mol. Diagn.* 2:145-152, Figeys and Pinto, 2001, *Electrophoresis* 2:208-216 and references in the publications listed here).

Complexes can be attached to an array by different means as will be apparent to a person skilled in the art. Complexes can for example be added to the array via a TAP-tag (as described in WO/0009716 and in Rigaut et al., 1999, *Nature Biotechnol.* 10:1030-1032) after the purification step or by another suitable purification scheme as will be apparent to a person skilled in the art.

Optionally, the proteins of the complex can be cross-linked to enhance the stability of the complex. Different methods to cross-link proteins are well known in the art. Reactive end-groups of cross-linking agents include but are not limited to -COOH, -SH, -NH<sub>2</sub> or N-oxy-succinamate.



The spacer of the cross-linking agent should be chosen with respect to the size of the complex to be cross-linked. For small protein complexes, comprising only a few proteins, relatively short spacers are preferable in order to reduce the likelihood of cross-linking separate complexes in the reaction mixture. For larger protein complexes, additional use of larger spacers is preferable in order to facilitate cross-linking between proteins within the complex.

It is preferable to check the success-rate of cross-linking before linking the complex to the carrier.

As will be apparent to a person skilled in the art, the optimal rate of cross-linking need to be determined on a case by case basis. This can be achieved by methods well known in the art, some of which are exemplary described below.

A sufficient rate of cross-linking can be checked f.e. by analysing the cross-linked complex vs. a non-cross-linked complex on a denaturing protein gel.

If cross-linking has been performed successfully, the proteins of the complex are expected to be found in the same lane, whereas the proteins of the non-cross-linked complex are expected to be separated according to their individual characteristics. Optionally the presence of all proteins of the complex can be further checked by peptide-sequencing of proteins in the respective bands using methods well known in the art such as mass spectrometry and/or Edman degradation.

In addition, a rate of crosslinking which is too high should also be avoided. If cross-linking has been carried out too extensively, there will be an increasing amount of cross-linking of the individual protein complex, which potentially interferes with a screening for potential binding partners and/or modulators etc. using the arrays.

The presence of such structures can be determined by methods well known in the art and include e.g. gel-filtration experiments comparing the gel filtration profile solutions containing cross-linked complexes vs. uncross-linked complexes.

Optionally, functional assays as will be apparent to a person skilled in the art, some of which are exemplarily provided herein, can be performed to check the integrity of the complex.

Alternatively, members of the protein complex can be expressed as a single fusion protein and coupled to the matrix as will be apparent to a person skilled in the art.

Optionally, the attachment of the complex or proteins or antibody as outlined above can be further monitored by various methods apparent to a person skilled in the art. Those include, but are not limited to surface plasmon resonance (see e.g. McDonnell, 2001, *Curr. Opin. Chem. Biol.* 5:572-577; Lee, 2001, *Trends Biotechnol.* 19:217-222; Weinberger et al., 2000, 1:395-416; Pearson et al., 2000, *Ann. Clin. Biochem.* 37:119-145; Vely et al., 2000, *Methods Mol. Biol.* 121:313-321; Slepak, 2000, *J. Mol. Recognit.* 13:20-26.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Cao X et al., 2001, *Science*, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Vassar R et al., 1999, *Science*, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Yan R et al., 1999, *Nature*, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Fe65-complex include but are not limited to those described in Tian Gaochao et al., 2002, *J Biol Chem*, 277:31499-505.

Exemplary assays useful for measuring the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Biederer Thomas et al., 2002, *J Neurosci*, 22:7340-51.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the PSEN2 -complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the

PSEN2 -complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Nicastrin-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the



expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Aph-1a-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Pen-2-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Yan R et al., 1999, *Nature*, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the APP695SW-complex include but are not limited to those described in Tian Gaochao et al., 2002, *J Biol Chem*, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Cao X et al., 2001, *Science*, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Vassar R et al., 1999, *Science*, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Yan R et al., 1999, *Nature*, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the APP-C99 -complex include but are not limited to those described in Tian Gaochao et al., 2002, *J Biol Chem*, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-

C99 -complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau-complex include but are not limited to those described in Drewes G et al., 1997, Cell, 89:297-308.

Exemplary assays useful for measuring the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau-complex include but are not limited to those described in Barghorn S et al., 2000, Biochemistry, 39:11714-21.

#### 4.6.1 CANDIDATE MOLECULES

Any molecule known in the art can be tested for its ability to modulate (increase or decrease) the amount of, activity of, or protein component composition of a complex of the present invention as detected by a change in the amount of, activity of, or protein component composition of, said complex. By way of example, a change in the amount of the complex can be detected by detecting a change in the amount of the complex that can be isolated from a cell expressing the complex machinery. For identifying a molecule that modulates complex activity, candidate molecules can be directly provided to a cell expressing the complex machinery, or, in the case of candidate proteins, can be provided by providing their encoding nucleic acids under conditions in which the nucleic acids are recombinantly expressed to produce the candidate proteins within the cell expressing the complex machinery, the complex is then isolated from the cell and the isolated complex is assayed for activity using methods well known in the art, not limited to those described, supra.

This embodiment of the invention is well suited to screen chemical libraries for molecules which modulate, e.g., inhibit, antagonize, or agonize, the amount of, activity of, or protein component composition of the complex. The chemical libraries can be peptide libraries, peptidomimetic libraries, chemically synthesized libraries, recombinant,

e.g., phage display libraries, and in vitro translation-based libraries, other non-peptide synthetic organic libraries, etc.

Exemplary libraries are commercially available from several sources (ArQule, Tripos/PanLabs, ChemDesign, Pharmacopoeia). In some cases, these chemical libraries are generated using combinatorial strategies that encode the identity of each member of the library on a substrate to which the member compound is attached, thus allowing direct and immediate identification of a molecule that is an effective modulator. Thus, in many combinatorial approaches, the position on a plate of a compound specifies that compound's composition. Also, in one example, a single plate position may have from 1-20 chemicals that can be screened by administration to a well containing the interactions of interest. Thus, if modulation is detected, smaller and smaller pools of interacting pairs can be assayed for the modulation activity. By such methods, many candidate molecules can be screened.

Many diversity libraries suitable for use are known in the art and can be used to provide compounds to be tested according to the present invention. Alternatively, libraries can be constructed using standard methods. Chemical (synthetic) libraries, recombinant expression libraries, or polysome-based libraries are exemplary types of libraries that can be used.

The libraries can be constrained or semirigid (having some degree of structural rigidity), or linear or nonconstrained. The library can be a cDNA or genomic expression library, random peptide expression library or a chemically synthesized random peptide library, or non-peptide library. Expression libraries are introduced into the cells in which the assay occurs, where the nucleic acids of the library are expressed to produce their encoded proteins.

In one embodiment, peptide libraries that can be used in the present invention may be libraries that are chemically synthesized in vitro. Examples of such libraries are given in Houghten et al., 1991, *Nature* 354:84-86, which describes mixtures of free hexapeptides in which the first and second residues in each peptide were individually and specifically defined; Lam et al., 1991, *Nature* 354:82-84, which describes a "one bead, one peptide" approach in which a solid phase split synthesis scheme produced a library of peptides in which each bead in the collection had immobilized thereon a single, random sequence of amino acid residues; Medynski, 1994, *Bio/Technology* 12:709-710, which describes split synthesis and T-bag synthesis methods; and Gallop et al., 1994, *J. Med. Chem.* 37:1233-1251. Simply by way of other examples, a combinatorial library



may be prepared for use, according to the methods of Ohlmeyer et al., 1993, Proc. Natl. Acad. Sci. USA 90:10922-10926; Erb et al., 1994, Proc. Natl. Acad. Sci. USA 91:11422-11426; Houghten et al., 1992, Biotechniques 13:412; Jayawickreme et al., 1994, Proc. Natl. Acad. Sci. USA 91:1614-1618; or Salmon et al., 1993, Proc. Natl. Acad. Sci. USA 90:11708-11712. PCT Publication No. WO 93/20242 and Brenner and Lerner, 1992, Proc. Natl. Acad. Sci. USA 89:5381-5383 describe "encoded combinatorial chemical libraries," that contain oligonucleotide identifiers for each chemical polymer library member.

In a preferred embodiment, the library screened is a biological expression library that is a random peptide phage display library, where the random peptides are constrained (e.g., by virtue of having disulfide bonding).

Further, more general, structurally constrained, organic diversity (e.g., nonpeptide) libraries, can also be used. By way of example, a benzodiazepine library (see e.g., Bunin et al., 1994, Proc. Natl. Acad. Sci. USA 91:4708-4712) may be used.

Conformationally constrained libraries that can be used include but are not limited to those containing invariant cysteine residues which, in an oxidizing environment, cross-link by disulfide bonds to form cystines, modified peptides (e.g., incorporating fluorine, metals, isotopic labels, are phosphorylated, etc.), peptides containing one or more non-naturally occurring amino acids, non-peptide structures, and peptides containing a significant fraction of  $\gamma$ -carboxyglutamic acid.

Libraries of non-peptides, e.g., peptide derivatives (for example, that contain one or more non-naturally occurring amino acids) can also be used. One example of these are peptoid libraries (Simon et al., 1992, Proc. Natl. Acad. Sci. USA 89:9367-9371). Peptoids are polymers of non-natural amino acids that have naturally occurring side chains attached not to the  $\alpha$  carbon but to the backbone amino nitrogen. Since peptoids are not easily degraded by human digestive enzymes, they are advantageously more easily adaptable to drug use. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al., 1994, Proc. Natl. Acad. Sci. USA 91:11138-11142).

The members of the peptide libraries that can be screened according to the invention are not limited to containing the 20 naturally occurring amino acids. In particular, chemically synthesized libraries and polysome based libraries allow the use of amino acids in addition to the 20 naturally occurring amino acids (by their inclusion in the

precursor pool of amino acids used in library production). In specific embodiments, the library members contain one or more non-natural or non-classical amino acids or cyclic peptides. Non-classical amino acids include but are not limited to the D-isomers of the common amino acids,  $\alpha$ -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid;  $\gamma$ -Abu,  $\gamma$ -Ahx, 6-amino hexanoic acid; Aib, 2-amino isobutyric acid; 3-amino propionic acid; ornithine; norleucine; norvaline, hydroxyproline, sarcosine, citrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine,  $\beta$ -alanine, designer amino acids such as  $\beta$ -methyl amino acids,  $\gamma$ -methyl amino acids, N-methyl amino acids, fluoro-amino acids and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

In a specific embodiment, fragments and/or analogs of complexes of the invention, or protein components thereof, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex activity or formation.

In another embodiment of the present invention, combinatorial chemistry can be used to identify modulators of the complexes. Combinatorial chemistry is capable of creating libraries containing hundreds of thousands of compounds, many of which may be structurally similar. While high throughput screening programs are capable of screening these vast libraries for affinity for known targets, new approaches have been developed that achieve libraries of smaller dimension but which provide maximum chemical diversity. (See e.g., Matter, 1997, *J. Med. Chem.* 40:1219-1229).

One method of combinatorial chemistry, affinity fingerprinting, has previously been used to test a discrete library of small molecules for binding affinities for a defined panel of proteins. The fingerprints obtained by the screen are used to predict the affinity of the individual library members for other proteins or receptors of interest (in the instant invention, the protein complexes of the present invention and protein components thereof.) The fingerprints are compared with fingerprints obtained from other compounds known to react with the protein of interest to predict whether the library compound might similarly react. For example, rather than testing every ligand in a large library for interaction with a complex or protein component, only those ligands having a fingerprint similar to other compounds known to have that activity could be tested. (See, e.g., Kauvar et al., 1995, *Chem. Biol.* 2:107-118; Kauvar, 1995, *Affinity fingerprinting*, Pharmaceutical Manufacturing International. 8:25-28; and Kauvar, *Toxic-Chemical Detection by Pattern Recognition in New Frontiers in Agrochemical Immunoassay*, Kurtz, Stanker and Skeritt (eds), 1995, AOAC: Washington, D.C., 305-312).

Kay et al. (1993, Gene 128:59-65) disclosed a method of constructing peptide libraries that encode peptides of totally random sequence that are longer than those of any prior conventional libraries. The libraries disclosed in Kay et al. encode totally synthetic random peptides of greater than about 20 amino acids in length. Such libraries can be advantageously screened to identify complex modulators. (See also U.S. Patent No. 5,498,538 dated March 12, 1996; and PCT Publication No. WO 94/18318 dated August 18, 1994).

A comprehensive review of various types of peptide libraries can be found in Gallop et al., 1994, J. Med. Chem. 37:1233-1251.

#### 4.7 PHARMACEUTICAL COMPOSITIONS AND THERAPEUTIC/PROPHYLACTIC ADMINISTRATION

The invention provides methods of treatment (and prophylaxis) by administration to a subject of an effective amount of a therapeutic of the invention. In a preferred aspect, the therapeutic is substantially purified. The subject is preferably an animal including, but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human. In a specific embodiment, a non-human mammal is the subject.

Various delivery systems are known and can be used to administer a therapeutic of the invention, e.g., encapsulation in liposomes, microparticles, and microcapsules; use of recombinant cells capable of expressing the therapeutic, use of receptor-mediated endocytosis (e.g., Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432); construction of a therapeutic nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion, by bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral, rectal and intestinal mucosa, etc.), and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir,

such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment. This may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) of a malignant tumor or neoplastic or pre-neoplastic tissue.

In another embodiment, the therapeutic can be delivered in a vesicle, in particular a liposome (Langer, 1990, *Science* 249:1527-1533; Treat et al., 1989, In: *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler, eds., Liss, New York, pp. 353-365; Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the therapeutic can be delivered via a controlled release system. In one embodiment, a pump may be used (Langer, *supra*; Sefton, 1987, *CRC Crit. Ref. Biomed. Eng.* 14:201-240; Buchwald et al., 1980, *Surgery* 88:507-516; Saudek et al., 1989, *N. Engl. J. Med.* 321:574-579). In another embodiment, polymeric materials can be used (*Medical Applications of Controlled Release*, Langer and Wise, eds., CRC Press, Boca Raton, Florida, 1974; *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball, eds., Wiley, New York, 1984; Ranger and Peppas, 1983, *Macromol. Sci. Rev. Macromol. Chem.* 23:61; Levy et al., 1985, *Science* 228:190-192; During et al., 1989, *Ann. Neurol.* 25:351-356; Howard et al., 1989, *J. Neurosurg.* 71:858-863). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (e.g., Goodson, 1984, In: *Medical Applications of Controlled Release*, *supra*, Vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer (1990, *Science* 249:1527-1533).

In a specific embodiment where the therapeutic is a nucleic acid encoding a protein therapeutic, the nucleic acid can be administered *in vivo* to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle



bombardment (e.g., a gene gun; Biolistic, Dupont), or by coating it with lipids, cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (e.g., Joliot et al., 1991, Proc. Natl. Acad. Sci. USA 88:1864-1868), etc. Alternatively, a nucleic acid therapeutic can be introduced intracellularly and incorporated by homologous recombination within host cell DNA for expression.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a therapeutic, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for

proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated, in accordance with routine procedures, as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water or saline for injection can be provided so that the ingredients may be mixed prior to administration.

The therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free carboxyl groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., those formed with free amine groups such as those derived from isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc., and those derived from sodium, potassium, ammonium, calcium, and ferric hydroxides, etc.

The amount of the therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20-500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. For example, the kit can comprise in one or more containers a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins listed in the fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1.

Alternatively, the kit can comprise in one or more containers, all proteins, functionally active fragments or functionally active derivatives thereof of from the group of proteins in the sixth column of table 1.

The kits of the present invention can also contain expression vectors encoding the essential components of the complex machinery, which components after being expressed can be reconstituted in order to form a biologically active complex. Such a kit preferably also contains the required buffers and reagents. Optionally associated with such container(s) can be instructions for use of the kit and/or a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

#### 4.8 ANIMAL MODELS

The present invention also provides animal models. In one embodiment, animal models for diseases and disorders involving the protein complexes of the present invention are provided. These animal models are well known in the art. These animal models include,

but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention. Such animals can be initially produced by promoting homologous recombination or insertional mutagenesis between genes encoding the protein components of the complexes in the chromosome, and exogenous genes encoding the protein components of the complexes that have been rendered biologically inactive or deleted (preferably by insertion of a heterologous sequence, e.g., an antibiotic resistance gene). In a preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which a gene encoding a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a gene encoding a component protein from the fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, has been inactivated or deleted (Capecchi, 1989, Science 244:1288-1292).

In another preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which the genes of all component proteins from the group of proteins listed in the fourth column of table 1 or of all proteins from the group of proteins listed in the fifth column of table 1 have been inactivated or deleted.

The chimeric animal can be bred to produce additional knockout animals. Such animals can be mice, hamsters, sheep, pigs, cattle, etc., and are preferably non-human mammals. In a specific embodiment, a knockout mouse is produced.

Such knockout animals are expected to develop, or be predisposed to developing, diseases or disorders associated with mutations involving the protein complexes of the present invention, and thus, can have use as animal models of such diseases and disorders, e.g., to screen for or test molecules (e.g., potential therapeutics) for such diseases and disorders.

In a different embodiment of the invention, transgenic animals that have incorporated and express (or over-express or mis-express) a functional gene encoding a



protein component of the complex, e.g. by introducing the a gene encoding one or more of the components of the complex under the control of a heterologous promoter (i.e., a promoter that is not the native promoter of the gene) that either over-expresses the protein or proteins, or expresses them in tissues not normally expressing the complexes or proteins, can have use as animal models of diseases and disorders characterized by elevated levels of the protein complexes. Such animals can be used to screen or test molecules for the ability to treat or prevent the diseases and disorders cited supra.

In one embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group of proteins listed in the fourth column of table 1, and an endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1 has been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof. In addition, the present invention provides a recombinant non-human animal in which the endogenous genes of all proteins, or functionally active fragments or functionally active derivatives thereof of one of the group of proteins listed in the sixth column have been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof:

In another embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins of the fourth column of table 1, and an endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins of the fifth column, of table 1 are recombinantly expressed in said animal or an ancestor thereof.

The following series of examples are presented by way of illustration and not by way of limitation on the scope of the invention.

## EXAMPLES

An object of the present invention was to identify protein complexes of the APP processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Those complexes are, as called herein, the following complexes:

Aph1a-complex, APP-695SW-complex, APP-C99-complex, Fe65-complex, Nicastrin-complex, Psen-2-complex, Pen2-complex, Tau-complex, X11 $\beta$ -complex

Thus, the invention relates to the following embodiments:

The present invention relates to the Fe65-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
    - (ii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
    - (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
    - (iv) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
  - (vi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and
  - (vii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
  - (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
  - (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
  - (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
  - (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,

- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (viii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (ix) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (x) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (xii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (xiii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xiv) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xv) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xvi) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and

(xvii) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Fe65 (SEQ ID NO. 13), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Fe65' encoded by a nucleic acid that hybridizes to the 'Fe65' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or



(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 16 of the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,



- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions,

(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex,

preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Fe65 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Fe65 complex selected from

- (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and
- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, wherein said low



stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
  - (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
  - (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
  - (iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Fe65 complex to one or more candidate molecules; and

- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.



30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions, and/or

- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the



complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether  
 (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or  
 (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or  
 (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .



42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins  
 (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,  
 (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,  
 (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein

- eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic

acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,

(xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,

(xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,

(xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

- (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,
- (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,
- (xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,
- (xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

The invention further relates to the following embodiments of the X11beta-complex:



1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
    - (ii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,
    - (iii) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
    - (iv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
    - (v) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and
    - (vi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (iv) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (v) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vi) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (vii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (viii) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2"

encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(xi) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

(xii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,

(xiii) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

(xiv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xv) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xvi) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

- (xvii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xviii) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xix) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,
- (xx) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xxi) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,
- (xxii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,
- (xxiii) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,
- (xxiv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that



hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxv) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxvii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxiii) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxv) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxvi) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xl) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xli) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xlii) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xliii) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xliv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlv) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlvi) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

- (xlviii) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (xlix) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (l) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (li) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (lii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (liii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,
- (liv) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,
- (lv) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the



"Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(lvi) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(lvii) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(lviii) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,

(lix) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,

(lx) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(lxi) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(lxiii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that

- hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,
- (lxiv) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,
- (lxv) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,
- (lxvi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,
- (lxvii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,
- (lxviii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,
- (lxix) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,
- (lxx) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and

(lxxi) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein X11beta (SEQ ID NO. 96), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'X11beta' encoded by a nucleic acid that hybridizes to the 'X11beta' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,



- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)"

- encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,
- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2

protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,



(xlili) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1"

- encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,
- (lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,
- (lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,
- (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2"

encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(lxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(lxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,



(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, and a protein complex selected from complex (II) and comprising the following proteins:

(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

(ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a

nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic

- acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,
- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154"



encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxiv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that

hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvi) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xli) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xlii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xlili) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a

nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlvi) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlvii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlviii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xlix) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(l) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(li) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a

nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(lii) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(liii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(liv) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(lv) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lvi) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(lvii) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(lviii) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,



- (lix) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lx) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (lxi) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxiii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,
- (lxiv) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,
- (lxv) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,
- (lxvi) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

- (Ixxvii) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,
- (Ixxviii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,
- (Ixxix) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,
- (Ixxx) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,
- (Ixxxi) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,
- (Ixxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 70 of the following proteins:

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

- homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,



(xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that

hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,



(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(i) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(ii) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,

(lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

- (lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,
- (lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,
- (lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,
- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,
- (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,

(lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,

(lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(lxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(lxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin

3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions,

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions.



5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the X11beta complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the X11beta complex selected from
  - (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
  - (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
  - (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
  - (iv) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
  - (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

- (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,
- (xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7



(FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and

(xxxiii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
  - (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
  - (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
  - (iv) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
  - (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
  - (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2"



encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that

hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48"

encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1"

encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

(ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a



nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(iv) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056"

encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a

nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or



(xxxiii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, comprising the steps of

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing X11beta complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of

said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions, and/or

- (vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein"

- encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a



nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

- variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions, and/or
- (xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or
- (xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions, and/or
- (xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056"

encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7

- (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or
- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a



nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or

(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions, and/or

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or

(lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or

(lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions, and/or

- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or
- (lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions, and/or
- (lxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

- (Ixxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions, and/or
- (Ixxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions, and/or
- (Ixxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to

the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity,



or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether  
(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the

- "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions, and/or
  - (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions, and/or
  - (vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
  - (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
  - (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or
  - (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or
  - (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or
  - (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or

- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2



protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions, and/or

- (xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or
- (xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or
- (xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or
- (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

- (xlili) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or
- (xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or
- (xlvi) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1"

- encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or
- (lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or



- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or

- (I xvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions, and/or
- (I xviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or
- (I xix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions, and/or
- (I xx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or
- (I xxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions, and/or
- (I xxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, and/or
- (I xxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or
- (I xxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or

transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
  - (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
  - (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
  - (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
  - (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a



nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic

acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154"

- encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,
- (xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,



(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

- (xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,
- (xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

- (Ix) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (Ixi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (Ixii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (Ixiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (Ixiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
- (Ixv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (Ixvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (Ixvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,
- (Ixviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a



variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(lxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or (lxxvii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

The present invention further relates to the following embodiments of the Presenilin-2 complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
    - (ii) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
    - (iii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and
    - (iv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2"

encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a

- nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xi) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiii) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xiv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a



nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvi) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xvii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xviii) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xix) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xx) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxi) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

(xxii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,

(xxiii) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xxv) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xxvi) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,
- (xxvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xxviii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (xxix) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (xxx) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-

glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxii) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxiii) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxv) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxxix) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xl) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xli) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xlii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xliii) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xliv) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,
- (xlv) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,
- (xlvi) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex"



encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlvii) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(xlix) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(l) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(li) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(lii) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(liii) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(liv) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

- (lv) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (lvi) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (lvii) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (lviii) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (lix) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,
- (lx) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (lxii) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,
- (lxiii) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6"

encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxiv) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxv) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxix) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxi) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

- (lxxii) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,
- (lxxiii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,
- (lxxiv) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,
- (lxxv) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,
- (lxxvi) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,
- (lxxvii) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,
- (lxxviii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,
- (lxxix) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, (lxxx) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxii) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and

(lxxxiii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein "Presenilin-2" (SEQ ID NO. 172), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Presenilin-2'

encoded by a nucleic acid that hybridizes to the 'Presenilin-2' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,

- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,
- (xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,
- (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,
- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,
- (xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,



- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,
- (xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

- (xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,
- (xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,
- (xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a

nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6"



encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,

(lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(Ixm) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(Ixiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(Ixv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(Ixvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(Ixvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(Ixviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(Ixix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(Ixx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(Ixxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2"

encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or



(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 82 of the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic

- acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1"

encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,

(xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,

(xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420"



encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlvii) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlix) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(li) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(lii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(liii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(liiii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,
- (lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,
- (lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2"



encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

- (lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,
- (lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,
- (lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,
- (lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,
- (lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,
- (lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,
- (lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

- (lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,
- (lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,
- (lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,
- (lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,
- (lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions,
- (lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,
- (lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,
- (lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3"

encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, (lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).



9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Presenilin 2 complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the Presenilin 2 complex selected from
- (i) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,
  - (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
  - (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
  - (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic

acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or



(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342"

encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(x) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,
- (xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA



INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,
- (xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.



26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Presenilin 2 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions, and/or

(iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions, and/or

(iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or

(v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions, and/or

(vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the

"Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or

(x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51"

encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions, and/or



- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or
- (xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions, and/or
- (xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or
- (xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or
- (xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

- (xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions, and/or
- (xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions, and/or
- (xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions, and/or

- (xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or
- (xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or
- (xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or
- (xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions, and/or

- (xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions, and/or
- (xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or
- (li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or



- (lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3"

- encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or
- (lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or
- (lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or
- (lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or
- (lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or
- (lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or
- (lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

- (lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or
- (lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or
- (lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or
- (lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions, and/or
- (lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions, and/or
- (lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that

hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or



(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or

- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, and/or



- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248"

encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

.(l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or

(li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a



nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions, and/or

(lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions, and/or

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or

(lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or

(lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or

(lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions, and/or

(lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or

- (Ix) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or
- (Ixi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or
- (Ixiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or
- (Ixiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or
- (Ixv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or
- (Ixvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or
- (Ixvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11"

encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or

(lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a



variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi

(siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins  
 (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,  
 (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,  
 (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,  
 (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a

nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,

(xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,

(xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic



acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,

(xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,

(xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1"

encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xlili) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

- (xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,
- (xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,
- (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,
- (li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,



(lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,

(lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a

nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(Ixxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(Ixx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(Ixxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(Ixxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(Ixxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(Ixxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,



(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions,

and/or(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Nicastrin-complex:

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
    - (ii) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
    - (iii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin"

encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iv) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(v) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and

(vi) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(v) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(vi) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(vii) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(viii) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(ix) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(x) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

(xi) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xii) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

- (xiii) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xiv) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xviii) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xix) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxiv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxv) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxvii) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxi) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xxxvi) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and

(xxxvii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Nicastrin' (SEQ ID NO. 147), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Nicastrin' encoded by a nucleic acid that hybridizes to the 'Nicastrin' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid

that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,

(vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B"



encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

(xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

(xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,

(xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,

(xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

- (xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,
- (xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

- (xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,
- (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,
- (xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,



(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vi) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(vii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(viii) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(ix) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(x) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(xi) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

(xii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xiii) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

- (xiv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xv) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xix) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxvii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxviii) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxix) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxx) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1"



encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxv) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxvi) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xxxix) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xl) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 36 of the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,
- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,
- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390"



encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin"

encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein

yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions,

(xlili) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by



modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Nicastrin complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Nicastrin complex selected from

(i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

- (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,
- (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING

finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and

(xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the

nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof; selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,



or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

(vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

- (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,
- (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,
- (xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, comprising the steps of
  - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Nicastrin complex to one or more candidate molecules; and



(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether  
(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or  
(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions, and/or

(viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions, and/or

- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or



(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2"

encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes

to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or



- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein

kinase II beta chain" nucleic acid or its complement under low stringency conditions, and/or

(x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or

(xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions, and/or

(xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342"

encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or

(xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that

hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or



- (xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or
- (xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions, and/or
- (xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, and/or
- (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xlili) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,

(vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,



- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095"

- encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase"

encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein"

encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as



neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Aph1a-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
    - (ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
    - (iii) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
    - (iv) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
    - (v) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid

that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,

(v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

(viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,

- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xiv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xv) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

- (xvii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xviii) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xx) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (xxiii) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxiv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,



(xxv) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvi) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxvii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxviii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiii) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxv) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xi) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xliv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlv) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xlvi) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlvii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

- (xlviii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xlix) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (l) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lv) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,



- (lvi) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (lxii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

- (lxiv) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (lxv) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,
- (lxvi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,
- (lxvii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxviii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,
- (lxix) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,
- (lxx) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (lxxi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic

acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,

(lxxiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxv) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxviii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxix) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxx) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and

(lxxxii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Aph1a' (SEQ ID NO. 109), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Aph1a' encoded by a nucleic acid that hybridizes to the 'Aph1a' under low stringency conditions.



3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the

- "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,
- (xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,
- (xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a



variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlv) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xlvi) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlvii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlviii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin



7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,

(lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

(lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,

(lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

- (lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,
- (lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,
- (lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,
- (lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,
- (lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that

hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,



- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,



(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

- (xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,
- (xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,
- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

- (lx) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (lxi) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lxii) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxiv) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (lxv) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxvi) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,
- (lxvii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain



dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(Ixxix) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(Ixx) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixxxi) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(Ixxii) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(Ixxv) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,
- (lxxvi) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (lxxvii) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,
- (lxxviii) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,
- (lxxix) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,
- (lxxx) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (lxxxi) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,
- (lxxxii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 81 of the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid

- that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
  - (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
  - (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
  - (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
  - (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
  - (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
  - (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
  - (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the



"Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

(xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4"

encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2"

encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763"



encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a

nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,

(lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma"

encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,

(lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,

(lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

- (lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,
- (lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,
- (lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,
- (lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,
- (lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1"



encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP

- synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,
- (lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,
- (lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,
- (lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions,
- (lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Aph-1a complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the Aph-1a complex selected from
  - (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
  - (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
  - (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
  - (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
  - (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
  - (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral



protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xix) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10"

encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,
- (ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,



- (xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xix) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

- (xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

- (xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

- (xxxvi) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,
- (xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:



- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the

"HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

- (ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xix) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

- (xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,



- (xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to

the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Aph-1a complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
  - (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions, and/or
  - (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
  - (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions, and/or

- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or



- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

- (xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or
- (xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or
- (xlili) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or



- (xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions, and/or
- (xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or
- (xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or
- (xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or
- (l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions, and/or

- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions, and/or
- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions, and/or

- (Ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (Ixi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (Ixiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions, and/or
- (Ixiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, and/or
- (Ixv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or
- (Ixvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or
- (Ixvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions, and/or
- (Ixviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, and/or

(Ixxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(Ixx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(Ixxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(Ixxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(Ixxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, and/or

(Ixxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, and/or



(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament

for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or



- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions, and/or

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the

"Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that



hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or

- (xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or
- (xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or
- (l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions, and/or

- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin

- 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or
- (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or
- (lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions, and/or
- (lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, and/or
- (lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or
- (lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or



- (lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions, and/or
- (lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or
- (lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, and/or
- (lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, and/or
- (lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or
- (lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that

- hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, and/or
- (lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions, and/or
- (lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions, and/or
- (lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions, and/or
- (lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of

RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a



nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

(viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,

(ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,

(x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,

(xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

(xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a

nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the

"HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,



(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

- (xiv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,
- (xlv) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,
- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,



(lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic

acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions,

and/or(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Pen-2.complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iii) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and

(iv) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,

(ii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(iii) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(iv) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,

(v) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1



catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(vi) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(vii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(viii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(ix) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(x) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and

(xi) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Pen-2' (SEQ ID NO. 209), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Pen-2' encoded by a nucleic acid that hybridizes to the 'Pen-2' under low stringency conditions.
3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
  - (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
  - (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
  - (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
  - (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
  - (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
  - (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
  - (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102

(Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iii) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,



- (ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (x) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xi) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiii) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 10 of the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,

(vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions,
- (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Pen-2 complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the Pen-2 complex selected from
  - (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and

(iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

(iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Pen-2 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.



29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1

catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

(vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether  
(i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or



- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1"

encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,

(ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,

(vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803"

encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.



The present invention further relates to the following embodiments of the APP695SW-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
    - (ii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
    - (iii) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
    - (iv) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and
    - (v) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
    - (ii) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a

nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(iii) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(iv) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(v) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and

(vi) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'APP695SW' (SEQ ID NO. 290), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'APP695SW' encoded by a nucleic acid that hybridizes to the 'APP695SW' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that

hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a



nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 5 of the following proteins:

(i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773"

encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha"

encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the APP695SW complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the APP695SW complex selected from  
(i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or



(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, comprising the steps of  
(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and  
(b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8

comprising the steps of (a) exposing said complex, or a cell or organism containing APP695SW complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or



- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not

having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as

neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins  
 (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,  
 (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773"



encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha"

encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the APP-C99-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
    - (ii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
    - (iii) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and
    - (iv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid

that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iii) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(iv) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(v) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(vi) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(vii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,

(viii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(ix) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1

related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

(x) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

(xi) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xii) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein APP-C99 (SEQ ID NO. 10), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'APP-C99' encoded by a nucleic acid that hybridizes to the 'APP-C99' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:



- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102

(Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,

(xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

(xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

(xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or



(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 12 of the following proteins:

(i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that

- hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the APP-C99 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the APP-C99 complex selected from

(i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and

(iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442"



encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and

an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022"

encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing APP-C99 complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid



that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949"

encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or

(x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated

complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or



- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or

- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting

proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,



(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the following embodiments of the Tau-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
    - (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
    - (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
    - (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin"

encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,

(v) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(vi) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(vii) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(viii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and

(ix) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,

(ii) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,

(iii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,

(iv) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and

(v) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Tau (SEQ ID NO. 315), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Tau' encoded by a nucleic acid that hybridizes to the 'Tau' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-



repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 4 of the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-

repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.



12. Component of the Tau complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Tau complex selected from

(i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or

functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Tau complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions, and/or



- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA

regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity,

or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin"

encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or

(v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions, and/or

(vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)"



encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or  
 (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins
- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
  - (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
  - (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
  - (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
  - (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
  - (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
  - (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a

nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,

(viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or (xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

## 5. PROTOCOLS:

The TAP-technology, which is more fully described in EP 1 105 508 B1 and in Rigaut, et al., 1999, Nature Biotechnol. 17:1030-1032 respectively was used and further adapted as described below for protein purification. Proteins were identified using mass spectrometry as described further below.

### 5.1 Construction of TAP-tagged bait

The cDNAs encoding the complete ORF were obtained by RT-PCR. Total RNA was prepared from appropriate cell lines using the RNeasy Mini Kit (Qiagen). Both cDNA synthesis and PCR were performed with the SUPERScript One-Step RT-PCR for Long templates Kit (Life Technologies) using gene-specific primers. After 35-40 cycles of amplification PCR-products with the expected size were gel-purified with the MinElute PCR Purification Kit (Qiagen) and, if necessary, used for further amplification. Low-abundant RNAs were amplified by nested PCR before gel-purification. Restriction sites for NotI were attached to PCR primers to allow subcloning of amplified cDNAs into the retroviral vectors pLE94-N/C-TAP thereby generating N- or C-terminal fusions with the TAP-tag (Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032). N-terminal tagging was chosen for the following baits/entry points: Presenilin 2, Aph-1a, Pen-2, APP, Tau, Fe65. C-terminal tagging was chosen for the following baits/entry points: Nicastrin, Aph-1a, Aph-1b, APP695SW, APP-C99, Fe65, X11beta.

Clones were analyzed by restriction digest, DNA sequencing and by in vitro translation using the TNT T7 Quick Coupled Transcription/Translation System (Promega inc.). The presence of the proteins was proven by Western blotting using the protein A



part of the TAP-tag for detection. Briefly, separation of proteins by standard SDS-PAGE was followed by semi-dry transfer onto a nitrocellulose membrane (PROTRAN, Schleicher&Schuell) using the MultiphorII blotting apparatus from Pharmacia Biotech. The transfer buffer consisted of 48 mM Tris, 39 mM glycine, 10% methanol and 0,0375% sodium dodecylsulfate. After blocking in phosphate-buffered saline (PBS) supplemented with 10% dry milk powder and 0,1% Tween 20 transferred proteins were probed with the Peroxidase-Anti-Peroxidase Soluble Complex (Sigma) diluted in blocking solution. After intensive washing immunoreactive proteins were visualized by enhanced chemiluminescence (ECL; Amersham Pharmacia Biotech).

## 5.2 Preparation of Virus and infection

As a vector, a MoMLV-based recombinant virus was used.

The preparation has been carried out as follows:

### 5.2.1 Preparation of Virus

293 gp cells were grown to 100% confluency. They were split 1:5 on poly-L-Lysine plates (1:5 diluted poly-L-Lysine [0.01% stock solution, Sigma P-4832] in PBS, left on plates for at least 10 min.). On Day 2, 63 microgram of retroviral Vector DNA together with 13 microgram of DNA of plasmid encoding an appropriate envelope protein were transfected into 293 gp cells (Somia, et al., 1999, Proc. Natl. Acad. Sci. USA 96:12667-12672; Somia, et al. 2000, J. Virol. 74:4420-4424). On Day 3, the medium was replaced with 15 ml DMEM + 10% FBS per 15-cm dish. On Day 4, the medium containing viruses (supernatant) was harvested (at 24 h following medium change after transfection). When a second collection was planned, DMEM 10 % FBS was added to the plates and the plates were incubated for another 24 h. All collections were done as follows: The supernatant was filtered through 0.45 micrometer filter (Corning GmbH, cellulose acetate, 431155). The filter was placed into konical polyallomer centrifuge tubes (Beckman, 358126) that are placed in buckets of a SW 28 rotor (Beckman). The filtered supernatant was ultracentrifuged at 19400 rpm in the SW 28 rotor, for 2 hours at 21 degree Celsius. The supernatant was discarded. The pellet containing viruses was

resuspended in a small volume (for example 300 microliter) of Hank's Balanced Salt Solution [Gibco BRL, 14025-092], by pipetting up and down 100-times, using an aerosol-safe tip. The viruses were used for transfection as described below.

### 5.2.2 Infection

Cells that were infected were plated one day before into one well of a 6-well plate. 4 hours before infection, the old medium on the cells was replaced with fresh medium. Only a minimal volume was added, so that the cells are completely covered (e.g. 700 microliter). During infection, the cells were actively dividing.

A description of the cells and their growth conditions is given in 5.2.3

To the concentrated virus, polybrene (Hexadimethrine Bromide; Sigma, H 9268) was added to achieve a final concentration of 8 microgram/ml (this is equivalent to 2.4 microliter of the 1 milligram/ml polybrene stock per 300 microliter of concentrated retrovirus). The virus was incubated in polybrene at room temperature for 1 hour. For infection, the virus/polybrene mixture was added to the cells and incubated at 37 degree Celsius at the appropriate CO<sub>2</sub> concentration for several hours (e.g. over-day or over-night). Following infection, the medium on the infected cells was replaced with fresh medium. The cells were passaged as usual after they became confluent. The cells contain the retrovirus integrated into their chromosomes and stably express the gene of interest.

### 5.2.3 Cell lines

The following Cell-lines were used:

Fe65-complex: HEK-293-cells, SKN-BE2-cells, SH-SY5Y-cells; X11beta-complex: HEK-293-cells, SKN-BE2-cells, SH-SY5Y-cells; Psen-2-complex: SKN-BE2-cells, SH-SY5Y-cells, LAN-cells; Nicastrin-complex: HEK-293-cells, SKN-BE2-cells; Aph-1a-complex: HEK-293-cells, SKN-BE2-cells; Pen-2-complex: HEK-293-cells, SKN-BE2-cells;

APP695SW-complex: HEK-293-cells, SKN-BE2-cells; APP-C99-complex: SKN-BE2-cells; Tau-complex: SKN-BE2-cells, SH-SY5Y-cells

SKN-BE2 cells (American Type Culture Collection-No. CRL-2271) were grown in 95% OptiMEM + 5% iron-supplemented calf serum.

SH-SY5Y-cells were grown in 85% DMEM/F-12, 15% FBS, Non-essential AA

LAN-cells (human neuroblastoma cell line) were grown in 90% RPMI 1640 + 10% FBS

The expression pattern of the TAP-tagged proteins was checked by immunoblot-analysis as described in 5.3.3 and/or by immunofluorescence as described in 5.3.1 or 5.3.2.

### 5.3 Checking of expression pattern of TAP-tagged proteins

The expression pattern of the TAP-tagged protein was checked by immunoblot analysis and/or by immunofluorescence. Immunofluorescence analysis was either carried out according to section 5.3.1 or to section 5.3.2 depending on the type of the TAP-tagged protein. Immunoblot analysis was carried out according to section 5.3.3.

#### 5.3.1 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for plasma membrane and ER bound proteins

Cells were grown in FCS media on polylysine coated 8 well chamber slides to 50% confluency. Then fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4). The cells were incubated for 30 minutes at room temperature in 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Blocking was performed with 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at room temperature. Incubation of the primary antibodies was performed in the blocking solution overnight at +4°C. The proper dilution of the antibodies was determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin for 2x 20 minutes at room temperature. Incubation of the

secondary antibodies is performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes). Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin was used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were then washed again 2x 20 minutes at room temperature in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

### 5.3.2 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for non-plasma membrane bound proteins:

Cells were grown in FCS media on Polylysine coated 8 well chamber slides to 50% confluency. Fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4) for 30 minutes at Room Temperature (RT), 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Permeabilization of cells was done with 0.5% Triton X-100 in PBS for 10 minutes at room temperature. Blocking was then done in 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at RT (Blocking solution). Incubation of the primary antibodies was performed in the blocking solution, overnight at +4°C. The proper dilution of the antibodies has to be determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin, for 2x 20 minutes at RT. Incubation of the secondary antibodies was performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes), Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin is used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were washed 2x 20 minutes at RT in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

### 5.3.3 Immunoblot analysis



To analyze expression levels of TAP-tagged proteins, a cell pellet (from a 6-well dish) was lysed in 60  $\mu$ l DNase I buffer (5% Glycerol, 100 mM NaCl, 0.8 % NP-40 (IGEPAL), 5 mM magnesium sulfate, 100  $\mu$ g/ml DNase I (Roche Diagnostics), 50 mM Tris, pH 7.5, protease inhibitor cocktail) for 15 min on ice. Each sample was split into two aliquots. The first half was centrifuged at 13,000 rpm for 5 min. to yield the NP-40-extractable material in the supernatant; the second half (total material) was carefully triturated. 50  $\mu$ g each of the NP-40-extractable material and the total material are mixed with DTT-containing sample buffer for 30 min at 50°C on a shaker and separated by SDS polyacrylamide gel electrophoresis on a precast 4-12% Bis-Tris gel (Invitrogen). Proteins were then transferred to nitrocellulose using a semi-dry procedure with a discontinuous buffer system. Briefly, gel and nitrocellulose membrane were stacked between filter papers soaked in either anode buffer (three layers buffer A1 (0.3 M Tris-HCl) and three layers buffer A2 (0.03 M Tris-HCl)) or cathode buffer (three layers of 0.03 M Tris-HCl, pH 9.4, 0.1 % SDS, 40 mM  $\epsilon$ -aminocaproic acid). Electrotransfer of two gels at once was performed at 600 mA for 25 min. Transferred proteins were visualized with Ponceau S solution for one min to control transfer efficiency and then destained in water. The membrane was blocked in 5% non-fat milk powder in TBST (TBS containing 0.05% Tween-20) for 30 min at room temperature. It was subsequently incubated with HRP-coupled PAP antibody (1:5000 diluted in 5% milk/TBST) for 1 h at room temperature, washed three times for 10 min in TBST. The blot membrane was finally soaked in chemiluminescent substrate (ECL, Roche Diagnostics) for 2 min. and either exposed to X-ray film or analyzed on an imaging station.

#### 5.4 Purification of protein complexes

Protein complex purification was adapted to the sub-cellular localization of the TAP-tagged protein and was performed as described below.

##### 5.4.1 Lysate preparation for cytoplasmic proteins

About  $1 \times 10^9$  adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid

nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of CZ lysis buffer (50 mM Tris-Cl, pH 7.4; 5 % Glycerol; 0,2 % IGEPAL; 1.5 mM  $\text{MgCl}_2$ ; 100 mM NaCl; 25 mM NaF; 1 mM  $\text{Na}_3\text{VO}_4$ ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was incubated for 30 min on ice and spun for 10 min at 20,000g. The supernatant was subjected to an additional ultracentrifugation step for 1 h at 100,000g. The supernatant was recovered and rapidly frozen in liquid nitrogen or immediately processed further.

#### 5.4.2 Lysate preparation for membrane proteins

About  $1 \times 10^9$  adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Membrane-Lysis buffer (50 mM Tris, pH 7.4; 7.5 % Glycerol; 1 mM EDTA; 150 mM NaCl; 25 mM NaF; 1 mM  $\text{Na}_3\text{VO}_4$ ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 750g, the supernatant was recovered and subjected to an ultracentrifugation step for 1 h at 100,000g. The membrane pellet was resuspended in 7,5 ml of Membrane-Lysis buffer containing 0.8% n-Dodecyl- $\beta$ -D-maltoside and incubated for 1 h at 4°C with constant agitation. The sample was subjected to another ultracentrifugation step for 1h at 100,000g and the solubilized material was quickly frozen in liquid nitrogen or immediately processed further.

#### 5.4.3 Lysate preparation for nuclear proteins

About  $1 \times 10^9$  adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Hypotonic-Lysis buffer (10 mM Tris, pH 7.4; 1.5 mM  $\text{MgCl}_2$ ; 10 mM KCl; 25 mM NaF; 1 mM  $\text{Na}_3\text{VO}_4$ ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor

cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 2,000g and the resulting supernatant (S1) saved on ice. The nuclear pellet (P1) was resuspended in 5 ml Nuclear-Lysis buffer (50 mM Tris, pH 7.4; 1.5 mM MgCl<sub>2</sub>; 20 % Glycerol; 420 mM NaCl; 25 mM NaF; 1 mM Na<sub>3</sub>VO<sub>4</sub>; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and incubated for 30 min on ice. The sample was combined with S1, further diluted with 7 ml of Dilution buffer (110 mM Tris, pH 7.4; 0.7 % NP40; 1.5 mM MgCl<sub>2</sub>; 25 mM NaF; 1 mM Na<sub>3</sub>VO<sub>4</sub>; 1 mM DTT), incubated on ice for 10 min and centrifuged at 100,000g for 1h. The final supernatant (S2) was frozen quickly in liquid nitrogen.

#### 5.4.4 Tandem Affinity Purification

The frozen lysate was quickly thawed in a 37°C water bath, and spun for 20 min at 100,000g. The supernatant was recovered and incubated with 0.2 ml of settled rabbit IgG-Agarose beads (Sigma) for 2 h with constant agitation at 4°C. Immobilized protein complexes were washed with 10 ml of CZ lysis buffer (containing 1 Complete™ tablet (Roche) per 50 ml of buffer) and further washed with 5 ml of TEV cleavage buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 0.5 mM EDTA; 1 mM DTT). Protein-complexes were eluted by incubation with 5 µl of TEV protease (GibcoBRL, Cat.No. 10127-017) for 1 h at 16°C in 150 µl TEV cleavage buffer. The eluate was recovered and combined with 0.2 ml settled Calmodulin affinity beads (Stratagene) in 0.2 ml CBP binding buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 2mM MgAc; 2mM Imidazole; 1mM DTT; 4 mM CaCl<sub>2</sub>) followed by 1 h incubation at 4°C with constant agitation. Immobilized protein complexes were washed with 10 ml of CBP wash buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 1mM MgAc; 1mM Imidazole; 1mM DTT; 2 mM CaCl<sub>2</sub>) and eluted by addition of 600 µl CBP elution buffer (10 mM Tris, pH 8.0; 5 mM EGTA) for 5 min at 37°C. The eluate was recovered in a siliconized tube and lyophilized. The remaining Calmodulin resin was boiled for 5 min in 50 µl 4x Laemmli sample buffer. The sample buffer was isolated, combined with the lyophilised fraction and loaded on a NuPAGE gradient gel (Invitrogen, 4-12%, 1.5 mm, 10 well).

#### 5.4.5 Isolation of the Sambiasin complex of the invention from mouse tissue

Two mouse forebrains (0.6314 g total wet weight) were lysed in 14 mls of 50 mM HEPES pH 7.4; 150 mM NaCl; 1 mM EDTA; 0.5 mM Sodium Vanadate; 10% Glycerol; 1% n-Dodecyl- $\beta$ -D-maltoside containing standard proteinase inhibitors. The tissue was homogenised in a Warring blender for 30 seconds on ice. Homogenates were incubated on ice for 1 hour and then centrifuged at 13,000 g for 30 min at 4°C. The resulting pellet was stored at -80°C while the supernatant was centrifuged at 50,000 g for 30 min at 4°C and the resulting pellet was also stored at -80°C. 6.5 ml of the supernatant from this second centrifugation step was taken and combined with 25  $\mu$ l of anti presenilin-1 antisera (MAB5232, Chemicon). The antibody/lysate mixture was incubated for 1 hour at 4°C with end-over end mixing. Pre-washed protein G sepharose was added and the mixture was incubated overnight at 4°C with end-over mixing. The protein G was recovered by centrifugation at 200 g for 5 min at 4°C. The protein G beads were then washed 5 times in 1ml lysis buffer (containing 0.1% n-Dodecyl- $\beta$ -D-maltoside rather than 1%). 100  $\mu$ l of NuPAGE sample buffer (Invitrogen) was added and the sample incubated at 37°C for 10 min. Samples were separated on 4-12 % NuPAGE bis/tris gels (Invitrogen, 1.5 mm, 10 well). Proteins were visualized by staining with colloidal coomassie (Sigma) and then analysed by LC/MSMS.

#### 5.5 Protein identification by mass spectrometry

##### 5.5.1 Protein digestion prior to mass spectrometric analysis

Gel-separated proteins were reduced, alkylated and digested in gel essentially following the procedure described by Shevchenko et al., 1996, Anal. Chem. 68:850-858. Briefly, gel-separated proteins were excised from the gel using a clean scalpel, reduced using 10 mM DTT (in 5mM ammonium bicarbonate, 54°C, 45 min) and subsequently alkylated with 55 mM iodoacetamid (in 5 mM ammonium bicarbonate) at room temperature in the dark (30 min). Reduced and alkylated proteins were digested in gel with porcine trypsin (Promega) at a protease concentration of 12.5 ng/ $\mu$ l in 5mM ammonium bicarbonate. Digestion was allowed to proceed for 4 hours at 37°C and the reaction was subsequently stopped using 5  $\mu$ l 5% formic acid.



### 5.5.2 Sample preparation prior to analysis by mass spectrometry

Gel plugs were extracted twice with 20  $\mu$ l 1% TFA and pooled with acidified digest supernatants. Samples were dried in a vacuum centrifuge and resuspended in 13  $\mu$ l 1% TFA.

### 5.5.3 Mass spectrometric data acquisition

Peptide samples were injected into a nano LC system (CapLC, Waters or Ultimate, Dionex) which was directly coupled either to a quadrupole TOF (QTOF2, QTOF Ultima, QTOF Micro, Micromass or QSTAR Pulsar, Sciex) or ion trap (LCQ Deca XP) mass spectrometer. Peptides were separated on the LC system using a gradient of aqueous and organic solvents (see below). Solvent A was 5% acetonitrile in 0.5% formic acid and solvent B was 70% acetonitrile in 0.5% formic acid.

Time (min)	% solvent A	% solvent B
0	95	5
5.33	92	8
35	50	50
36	20	80
40	20	80
41	95	5
50	95	5

Peptides eluting off the LC system were partially sequenced within the mass spectrometer.

### 5.5.4 Protein identification

The peptide mass and fragmentation data generated in the LC-MS/MS experiments were used to query fasta formatted protein and nucleotide sequence databases maintained and updated regularly at the NCBI (for the NCBI nr, dbEST and the

human and mouse genomes) and European Bioinformatics Institute (EBI, for the human, mouse, *D. melanogaster* and *C. elegans* proteome databases). Proteins were identified by correlating the measured peptide mass and fragmentation data with the same data computed from the entries in the database using the software tool Mascot (Matrix Science; Perkins et al., 1999, *Electrophoresis* 20:3551-3567). Search criteria varied depending on which mass spectrometer was used for the analysis.

TABLE 1

## COMPONENTS OF COMPLEXES

Name of complex	Entry Point	All interactors of the complex	Known interactors of the complex	Novel interactors of the complex	Proteins of unknown function
Fe65-complex	Fe65	APP	APP		
		14-3-3 protein epsilon		14-3-3 protein epsilon	
		14-3-3 protein beta/alpha		14-3-3 protein beta/alpha	
		14-3-3 protein eta		14-3-3 protein eta	
		14-3-3 protein gamma		14-3-3 protein gamma	
		14-3-3 protein tau		14-3-3 protein tau	
		14-3-3 protein zeta/delta		14-3-3 protein zeta/delta	
		APLP1	APLP1		
		APLP2	APLP2		
		APP-C99	APP-C99	APP-C99	APP-C99
		ATP-binding cassette, sub-family B, member 7		ATP-binding cassette, sub-family B, member 7	

		ECP-51		ECP-51	
		Fe65	Fe65		
		GAP-associated tyrosine phosphoprotein p62		GAP-associated tyrosine phosphoprotein p62	
		Integral membrane protein 2B (ITM2B)		Integral membrane protein 2B (ITM2B)	
		IPI00104084.1		IPI00104084.1	IPI00104084.1
		Krab box protein ensp00000302970		Krab box protein ensp00000302970	Krab box protein ensp00000302970
		PDZ domain protein MAGI-3		PDZ domain protein MAGI-3	
		PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)		PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)	
		Protein similar to probable mitotic centromere associated kinesin		Protein similar to probable mitotic centromere associated kinesin	Protein similar to probable mitotic centromere associated kinesin
		RNB6	RNB6		
		SAP-62		SAP-62	
		Transcription factor CP2	Transcription factor CP2		



		Zinc finger protein 277		Zinc finger protein 277	Zinc finger protein 277
X11b-complex	X11b	ADAMTS-19		ADAMTS-19	ADAMTS-19
		APLP1		APLP1	
		APP	APP		
		Axonemal dynein heavy chain 8		Axonemal dynein heavy chain 8	
		BAT1		BAT1	BAT1
		C20orf11 (sim to a region of RANBPM)		C20orf11 (sim to a region of RANBPM)	C20orf11 (sim to a region of RANBPM)
		Cadherin EGF LAG seven-pass G-type receptor 2		Cadherin EGF LAG seven-pass G-type receptor 2	Cadherin EGF LAG seven-pass G-type receptor 2
		Calsyntenin-1		Calsyntenin-1	
		Calsyntenin-2		Calsyntenin-2	Calsyntenin-2
		Calsyntenin-3		Calsyntenin-3	Calsyntenin-3
		CGB0_HUMAN		CGB0_HUMAN	CGB0_HUMAN
		Chondroitin sulfate proteoglycan 6		Chondroitin sulfate proteoglycan 6	
		Chromatin-specific transcription elongation		Chromatin-specific transcription elongation	

		factor FACT 140 kDa subunit	factor FACT 140 kDa subunit	
		DC6 protein	DC6 protein	
		Dkfp586c1924	Dkfp586c1924	Dkfp586c1924
		Dynein light chain 2A	Dynein light chain 2A	
		Dynein light chain-A	Dynein light chain-A	
		ELAVL3	ELAVL3	
		ENG00000168820 (hypothetical protein with p-loop)	ENG00000168820 (hypothetical protein with p-loop)	ENG00000168820 (hypothetical protein with p-loop)
		Eukaryotic translation initiation factor 4A, isoform	Eukaryotic translation initiation factor 4A, isoform	
		Filamin, gamma	Filamin, gamma	
		FLJ13910	FLJ13910	FLJ13910
		FRAP1	FRAP1	
		GTP-binding protein ERA	GTP-binding protein ERA	
		HADH2/ERAB (mitochondrial enzyme)	HADH2/ERAB (mitochondrial enzyme)	
		HDAC2	HDAC2	
		HERC2 protein	HERC2 protein	HERC2 protein

	HSPC154		HSPC154	HSPC154
	HSPC245		HSPC245	HSPC245
	Hunc18a	Hunc18a		
	HYPOTHETICAL PROTEIN FLJ10618		HYPOTHETICAL PROTEIN FLJ10618	HYPOTHETICAL PROTEIN FLJ10618
	Hypothetical protein FLJ10795		Hypothetical protein FLJ10795	
	HYPOTHETICAL PROTEIN FLJ12599.		HYPOTHETICAL PROTEIN FLJ12599.	HYPOTHETICAL PROTEIN FLJ12599.
	Hypothetical protein FLJ20397		Hypothetical protein FLJ20397	Hypothetical protein FLJ20397
	hypothetical protein MGC13186		hypothetical protein MGC13186	hypothetical protein MGC13186
	IKAP		IKAP	
	Insulinoma-glucagonoma protein 20		Insulinoma- glucagonoma protein 20	
	KIAA0056		KIAA0056	KIAA0056
	KIAA0166		KIAA0166	KIAA0166
	KIAA0325 (FRAGMENT)		KIAA0325 (FRAGMENT)	
	KIAA0564		KIAA0564	KIAA0564

	KIAA0763		KIAA0763	KIAA0763
	Laminin, gamma 1		Laminin, gamma 1	
	LIB ( leucine-rich repeat protein)		LIB ( leucine-rich repeat protein)	
	MBIP		MBIP	
	MEGF7 (FRAGMENT)		MEGF7 (FRAGMENT)	MEGF7 (FRAGMENT)
	MT-ACT48		MT-ACT48	MT-ACT48
	Myosin IXB		Myosin IXB	
	NEU1		NEU1	
	Neurexin-1	Neurexin-1		
	NIPSNAP1		NIPSNAP1	NIPSNAP1
	NIPSNAP2		NIPSNAP2	
	Paladin		Paladin	Paladin
	PDZ and LIM domain protein 1		PDZ and LIM domain protein 1	PDZ and LIM domain protein 1
	Phosphoenolpyruvate carboxykinase 2 (mitochondrial)		Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	
	PILB		PILB	PILB
	PILT		PILT	PILT
	Procollagen C-		Procollagen C-	



	endopeptidase enhancer		endopeptidase enhancer	
	Programmed cell death 10		Programmed cell death 10	Programmed cell death 10
	Protein similar to AGCP6688		Protein similar to AGCP6688	Protein similar to AGCP6688
	RAB7L1		RAB7L1	RAB7L1
	RANBP1		RANBP1	
	Reelin		Reelin	
	RPGR-interacting protein 1		RPGR-interacting protein 1	
	Serine/threonine protein phosphatase 6		Serine/threonine protein phosphatase 6	
	similar to SD27354p [Drosophila melanogaster]		similar to SD27354p [Drosophila melanogaster]	similar to SD27354p [Drosophila melanogaster]
	SNAP-25	SNAP-25		
	Sortilin-related receptor		Sortilin-related receptor	
	STMN3		STMN3	
	STX1A	STX1A		
	SUCLA2		SUCLA2	
	Synaptogyrin 3		Synaptogyrin 3	

		TYK2		TYK2	
		Ubiquitin-protein ligase E3-alpha		Ubiquitin-protein ligase E3-alpha	Ubiquitin-protein ligase E3-alpha
		VGF nerve growth factor inducible protein		VGF nerve growth factor inducible protein	
		X11beta	X11beta		
		Zinc finger protein 198		Zinc finger protein 198	
PSEN2-complex	PSEN2	18 kDa microsomal signal peptidase subunit		18 kDa microsomal signal peptidase subunit	
		200 kDa proteasome activator		200 kDa proteasome activator	
		ABCB11		ABCB11	
		Acetolactate synthase homolog		Acetolactate synthase homolog	
		Adrenoleukodystrophy protein		Adrenoleukodystrophy protein	
		Aph-1a	Aph-1a		
		ATM		ATM	
		ATP7A		ATP7A	
		ATP-binding cassette protein, sub-family B,		ATP-binding cassette protein, sub-family B,	

		member 1		member 1	
		ATP-dependent metalloprotease FtsH1 homolog		ATP-dependent metalloprotease FtsH1 homolog	
		BIG1		BIG1	
		BTAF1		BTAF1	
		Calcium-binding protein P22		Calcium-binding protein P22	
		Cation-chloride cotransporter-interacting protein		Cation-chloride cotransporter- interacting protein	
		CD97		CD97	
		CDM_HUMAN		CDM_HUMAN	CDM_HUMAN
		Centromere/kinetochore protein ZW10 homolog		Centromere/kinetochore e protein ZW10 homolog	
		Cerebral protein 10		Cerebral protein 10	Cerebral protein 10
		CGI-13		CGI-13	CGI-13
		CGI-51		CGI-51	CGI-51
		cholinergic receptor, nicotinic, alpha polypeptide 3		cholinergic receptor, nicotinic, alpha polypeptide 3	

	CHRNA3		CHRNA3	
	DAAM1		DAAM1	
	DAPK1		DAPK1	
	DKFZp586c1924		DKFZp586c1924	DKFZp586c1924
	DOCK3		DOCK3	
	Down syndrome critical region protein 2		Down syndrome critical region protein 2	
	ECSIT		ECSIT	
	ensp00000297280 (hypothetical protein with p-loop)		ensp00000297280 (hypothetical protein with p-loop)	ensp00000297280 (hypothetical protein with p-loop)
	FACL1		FACL1	
	FLJ20342		FLJ20342	FLJ20342
	FLJ20420		FLJ20420	FLJ20420
	FLJ22555		FLJ22555	FLJ22555
	FLJ22678		FLJ22678	FLJ22678
	Galactosylgalactosylprotein 3-beta-glucuronosyltransferase 3		Galactosylgalactosylprotein 3-beta-glucuronosyltransferase 3	
	HTRA2		HTRA2	
	HU-K4		HU-K4	



		Hypothetical protein FLJ23356		Hypothetical protein FLJ23356	Hypothetical protein FLJ23356
		Hypothetical protein KIAA0455		Hypothetical protein KIAA0455	Hypothetical protein KIAA0455
		Hypothetical protein KIAA0971-I		Hypothetical protein KIAA0971-I	Hypothetical protein KIAA0971-I
		HYPOTHETICAL PROTEIN XP_174405.		HYPOTHETICAL PROTEIN XP_174405.	HYPOTHETICAL PROTEIN XP_174405.
		KIAA0062 (FRAGMENT)		KIAA0062 (FRAGMENT)	KIAA0062 (FRAGMENT)
		KIAA0090		KIAA0090	KIAA0090
		KIAA0103		KIAA0103	KIAA0103
		MGC4248		MGC4248	MGC4248
		MGC5442		MGC5442	MGC5442
		Nicastrin	Nicastrin		
		NICE-3		NICE-3	NICE-3
		NPC1		NPC1	
		NPD002		NPD002	
		NPL4, a component of the nuclear pore complex		NPL4, a component of the nuclear pore complex	NPL4, a component of the nuclear pore complex

		P63 protein			P63 protein	
		Presenilin 2		Presenilin 2		
		Prohibitin			Prohibitin	
		PSMA1			PSMA1	
		PSMA3			PSMA3	
		PSMA4			PSMA4	
		PSMA6			PSMA6	
		PSMB1			PSMB1	
		PSMB2			PSMB2	
		PSMB3			PSMB3	
		PSMB4			PSMB4	
		PSMB5			PSMB5	
		PSMB6			PSMB6	
		PSMC1			PSMC1	
		PSMC2			PSMC2	
		PSMC3			PSMC3	
		PSMC4			PSMC4	
		PSMC5			PSMC5	
		PSMC6			PSMC6	
		PSMD1			PSMD1	
		PSMD11			PSMD11	
		PSMD12			PSMD12	

		PSMD13		PSMD13	
		PSMD2		PSMD2	
		PSMD3		PSMD3	
		PSMD4		PSMD4	
		RPS6KA3		RPS6KA3	
		Serine/threonine protein phosphatase 6		Serine/threonine protein phosphatase 6	
		SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.		SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.	SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.
		Sortilin 1		Sortilin 1	
		Stearoyl-CoA desaturase		Stearoyl-CoA desaturase	
		STRA6 isoform 1		STRA6 isoform 1	STRA6 isoform 1
		Tparl		Tparl	Tparl
		Ubiquitin-protein ligase EDD		Ubiquitin-protein ligase EDD	
		Voltage-dependent anion channel 2		Voltage-dependent anion channel 2	
		Wolframin		Wolframin	
Nicastrin-	Nicastrin	18 kDa microsomal		18 kDa microsomal	

complex		signal peptidase subunit		signal peptidase subunit	
		25 kDa microsomal signal peptidase subunit		25 kDa microsomal signal peptidase subunit	
		Aph-1a	Aph-1a		
		ATP-binding cassette, sub-family A, member 3		ATP-binding cassette, sub-family A, member 3	ATP-binding cassette, sub-family A, member 3
		BACE1	BACE1		
		BSCv protein (FRAGMENT)		BSCv protein (FRAGMENT)	
		CAMK4		CAMK4	
		Casein kinase II beta chain		Casein kinase II beta chain	
		Cathepsin B		Cathepsin B	
		CGI-13		CGI-13	CGI-13
		DCTN1		DCTN1	
		Delta-6 fatty acid desaturase		Delta-6 fatty acid desaturase	
		ENSG00000144840		ENSG00000144840	ENSG00000144840
		FACL3		FACL3	



	FACL4			FACL4	
	FLJ13977			FLJ13977	
	FLJ20342			FLJ20342	FLJ20342
	FLJ20481			FLJ20481	FLJ20481
	FLJ22390			FLJ22390	FLJ22390
	homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)			homolog of yeast golgi membrane protein yip1p (yip1p-interacting factor)	
	ICAM-2			ICAM-2	
	KIAA0095			KIAA0095	KIAA0095
	KIAA0922			KIAA0922	KIAA0922
	KIAA1181 (FRAGMENT)			KIAA1181 (FRAGMENT)	KIAA1181 (FRAGMENT)
	KIAA1533 (FRAGMENT)			KIAA1533 (FRAGMENT)	KIAA1533 (FRAGMENT)
	Mesenchymal stem cell protein DSCD75			Mesenchymal stem cell protein DSCD75	
	Neurotrypsin			Neurotrypsin	
	Nicastrin		Nicastrin		
	NICE-3			NICE-3	
	PAS domain containing			PAS domain containing	

		serine/threonine kinase		serine/threonine kinase	
		Pen-2	Pen-2		
		PP1, regulatory subunit 15B		PP1, regulatory subunit 15B	PP1, regulatory subunit 15B
		Presenilin-1	Presenilin-1		
		Presenilin-2	Presenilin-2		
		Protein amplified in osteosarcoma (OS-9)		Protein amplified in osteosarcoma (OS-9)	
		Protein similar to stromal cell-derived factor 2		Protein similar to stromal cell-derived factor 2	
		Protocadherin beta 8		Protocadherin beta 8	
		REP8 protein		REP8 protein	
		Retinal short-chain dehydrogenase/reductase retSDR2		Retinal short-chain dehydrogenase/reductase retSDR2	
		RING finger protein 5		RING finger protein 5	RING finger protein 5
		Stromal cell-derived factor 2-like 1		Stromal cell-derived factor 2-like 1	
		Thioredoxin domain-containing protein		Thioredoxin domain-containing protein	Thioredoxin domain-containing protein
		tyrosine phosphatase		tyrosine phosphatase	tyrosine phosphatase

		ensg00000149185		ensg00000149185	ensg00000149185
Aph-1a-complex	Aph-1a	18 kDa microsomal signal peptidase subunit		18 kDa microsomal signal peptidase subunit	
		23 kDa microsomal signal peptidase		23 kDa microsomal signal peptidase	
		25 kDa microsomal signal peptidase subunit		25 kDa microsomal signal peptidase subunit	
		ABCC1		ABCC1	ABCC1
		Acetolactate synthase homolog		Acetolactate synthase homolog	Acetolactate synthase homolog
		APLP2		APLP2	
		Aph-1a	Aph-1a		
		APP		APP	
		ATM		ATM	
		ATP1B1		ATP1B1	
		ATP2C1		ATP2C1	
		ATP-binding cassette, sub-family A member 3		ATP-binding cassette, sub-family A member 3	ATP-binding cassette, sub-family A member 3
		Brain-specific GTP-		Brain-specific GTP-	

		binding protein		binding protein	
		CDW92		CDW92	CDW92
		Cerebral protein-10		Cerebral protein-10	Cerebral protein-10
		CGI-13		CGI-13	CGI-13
		CNTNAP1		CNTNAP1	
		Dihydrofolate reductase		Dihydrofolate reductase	
		DNM1		DNM1	
		Endocytic receptor		Endocytic receptor	
		Endo180		Endo180	
		ENG		ENG	
		EXT2		EXT2	
		EXTL3		EXTL3	
		FLJ13660		FLJ13660	
		GPR49		GPR49	GPR49
		HK2		HK2	
		HU-K4		HU-K4	
		HUNC18a		HUNC18a	
		HYPOTHETICAL PROTEIN		HYPOTHETICAL PROTEIN	HYPOTHETICAL PROTEIN
		Hypothetical protein (Fragment)		Hypothetical protein (Fragment)	Hypothetical protein (Fragment)



		Hypothetical protein FLJ14562		Hypothetical protein FLJ14562	Hypothetical protein FLJ14562
		Hypothetical protein FLJ23630		Hypothetical protein FLJ23630	Hypothetical protein FLJ23630
		Hypothetical protein KIAA0372		Hypothetical protein KIAA0372	Hypothetical protein KIAA0372
		hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5		hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5	hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5
		hypothetical protein MGC22916		hypothetical protein MGC22916	hypothetical protein MGC22916
		ICAM2		ICAM2	
		IGF2R		IGF2R	
		Insulinoma-glucagonoma protein 20		Insulinoma- glucagonoma protein 20	
		Integral membrane protein 2B (ITM2B)		Integral membrane protein 2B (ITM2B)	
		integral membrane transporter protein		integral membrane transporter protein	integral membrane transporter protein
		ITPR1		ITPR1	

		KIAA0062 (FRAGMENT)		KIAA0062 (FRAGMENT)	KIAA0062 (FRAGMENT)
		KIAA0251 (FRAGMENT)		KIAA0251 (FRAGMENT)	KIAA0251 (FRAGMENT)
		KIAA0363 (FRAGMENT)		KIAA0363 (FRAGMENT)	KIAA0363 (FRAGMENT)
		KIAA0763		KIAA0763	KIAA0763
		KIAA0971		KIAA0971	KIAA0971
		KIAA1250		KIAA1250	KIAA1250
		LRP5		LRP5	
		Mesenchymal stem cell protein DSCD75		Mesenchymal stem cell protein DSCD75	Mesenchymal stem cell protein DSCD75
		MGC4248		MGC4248	MGC4248
		Neurotrypsin		Neurotrypsin	
		Nicastrin	Nicastrin		
		NRP2		NRP2	
		PCDHA10		PCDHA10	PCDHA10
		PCDHB12		PCDHB12	PCDHB12
		PCDHB13:		PCDHB13:	PCDHB13:
		protocadherin beta 13		protocadherin beta 13	protocadherin beta 13
		Pcdhb17		Pcdhb17	Pcdhb17

	PCDHB4			PCDHB4	PCDHB4
	PCDHGB1			PCDHGB1	PCDHGB1
	PCDHGB6			PCDHGB6	PCDHGB6
	Pen-2		Pen-2		
	PMPCB			PMPCB	
	PP2C gamma			PP2C gamma	
	Presenilin 1		Presenilin 1		
	Presenilin 2		Presenilin 2		
	Protocadherin 7			Protocadherin 7	Protocadherin 7
	Protocadherin beta 16			Protocadherin beta 16	Protocadherin beta 16
	Protocadherin beta 8			Protocadherin beta 8	Protocadherin beta 8
	RAB-18			RAB-18	
	Rab3 GTPase-activating protein, non-catalytic subunit			Rab3 GTPase-activating protein, non-catalytic subunit	
	Retinal short-chain dehydrogenase/reductase retSDR2			Retinal short-chain dehydrogenase/reductase retSDR2	Retinal short-chain dehydrogenase/reductase retSDR2
	RNASEL			RNASEL	
	Sideroflexin 1			Sideroflexin 1	
	Signal transducer and			Signal transducer and	

		activator of transcription-1		activator of transcription-1	
		Similar to CGI-135 protein		Similar to CGI-135 protein	Similar to CGI-135 protein
		SMAP-1B		SMAP-1B	
		SPTLC2		SPTLC2	
		Sterile alpha and HEAT/Armadillo motif protein		Sterile alpha and HEAT/Armadillo motif protein	Sterile alpha and HEAT/Armadillo motif protein
		Sterol O-acyltransferase 1		Sterol O-acyltransferase 1	
		STMN3		STMN3	
		tegt: testis enhanced gene transcript (bax inhibitor 1)		tegt: testis enhanced gene transcript (bax inhibitor 1)	tegt: testis enhanced gene transcript (bax inhibitor 1)
		Thioredoxin domain-containing protein		Thioredoxin domain-containing protein	Thioredoxin domain-containing protein
		Triple functional domain protein (PTPRF interacting)		Triple functional domain protein (PTPRF interacting)	
		UNC5C		UNC5C	



		Vacuolar ATP synthase membrane sector associated protein m8-9		Vacuolar ATP synthase membrane sector associated protein m8-9	Vacuolar ATP synthase membrane sector associated protein m8-9
		vacuolar protein sorting protein 18		vacuolar protein sorting protein 18	
		Y391_HUMAN		Y391_HUMAN	Y391_HUMAN
Pen-2- complex	Pen-2	Alpha-2 catenin		Alpha-2 catenin	
		Aph-1a	Aph-1a		
		COPINE FAMILY MEMBER.		COPINE FAMILY MEMBER.	COPINE FAMILY MEMBER.
		Copine III		Copine III	
		Dachshund 2		Dachshund 2	
		Delta-1 catenin		Delta-1 catenin	
		KIAA1102 (Fragment)		KIAA1102 (Fragment)	KIAA1102 (Fragment)
		MGC2803		MGC2803	MGC2803
		Nicastrin	Nicastrin		
		Pen-2	Pen-2		
		Presenilin 1	Presenilin 1		
		Presenilin 2		Presenilin 2	

		TNRC15			TNRC15		TNRC15
		TPST1			TPST1		
		ZIP kinase			ZIP kinase		
APP695SW-complex	APP695S W	APP695SW		APP695SW			
		Fe65		Fe65			
		Fe65L1		Fe65L1			
		FLJ10773			FLJ10773	FLJ10773	
		GTF2I			GTF2I		
		IL13RA2			IL13RA2		
		Integral membrane protein 2B (ITM2B)			Integral membrane protein 2B (ITM2B)		
		Integral membrane transporter protein			Integral membrane transporter protein		
		JIP-1		JIP-1			
		S-100 alpha			S-100 alpha		
		X11beta		X11beta			
APP-C99-complex	APP-C99	APP			APP		
		APP-C99		APP-C99			
		CAMK2D			CAMK2D		
		Delta-like homolog			Delta-like homolog		

		Fe65	Fe65			
		Fe65L1	Fe65L1			
		Integral membrane transporter protein			Integral membrane transporter protein	
		KIAA1102 (Fragment)			KIAA1102 (Fragment)	KIAA1102 (Fragment)
		KIAA1949			KIAA1949	KIAA1949
		MGC4022			MGC4022	MGC4022
		MGC5442			MGC5442	MGC5442
		NAP-1 related protein			NAP-1 related protein	
		Neurocalcin delta			Neurocalcin delta	
		REST corepressor			REST corepressor	
		S-100 alpha			S-100 alpha	
		S-100 beta			S-100 beta	
		X11beta		X11beta		
Tau-complex	Tau	14-3-3 protein zeta/delta	14-3-3 protein zeta/delta			
		Actin	Actin			
		Alpha tubulin	Alpha tubulin			
		Beta tubulin	Beta tubulin			
		Deoxyhypusine synthase			Deoxyhypusine synthase	
		Dynactin 2			Dynactin 2	

		MEP50		MEP50	MEP50
		Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1		Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	
		PPP2CA (PP2A, catalytic subunit, alpha)	PPP2CA (PP2A, catalytic subunit, alpha)		
		PPP2CB (PP2A, catalytic subunit, beta)	PPP2CB (PP2A, catalytic subunit, beta)		
		PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)	PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)		
		PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)	PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)		
		S-100 beta		S-100 beta	
		Tau	Tau		



TABLE 2

## INDIVIDUAL PROTEINS OF THE COMPLEXES

Protein name	SEQ ID	IPI number	Molecular weight
14-3-3 protein epsilon	1	IPI00000816.1	29174
14-3-3 protein beta/alpha	2	IPI00216318.1	28082
14-3-3 protein eta	3	IPI00216319.1	28219
14-3-3 protein gamma	4	IPI00220642.1	28303
14-3-3 protein tau	5	IPI00018146.1	27764
14-3-3 protein zeta/delta	6	IPI00021263.1	27745
18 kDa microsomal signal peptidase subunit	100	IPI00104128.1	20625
200 kDa proteasome activator	101	IPI00005260.1	206407
23 kDa microsomal signal peptidase	221	IPI00030262.2	20253
25 kDa microsomal signal peptidase subunit	185	IPI00014148.1	25003
ABCB11	102	IPI00030011.1	146393
ABCC1	222	IPI00008338.1	164941
Acetolactate synthase homolog	107	IPI00009963.2	67868
Actin	305	IPI00021439.1	41737
ADAMTS-19	25	IPI00152639.1	134062
Adrenoleukodystrophy protein	108	IPI00017637.1	82909
Alpha tubulin	306	IPI00142632.1	50152

Alpha-2 catenin	280	IPI00030907.1	105282
Aph-1a	109	IPI00059964.1	28996
APLP1	7	IPI00020012.1	72176
APLP2	8	IPI00031030.1	86956
APP	9	IPI00006608.1	86943
APP695SW	290	CZB00000007.1	78630
APP-C99	10	CZB00000004.1	11277.9
ATM	103	IPI00012732.1	350644
ATP1B1	223	IPI00006484.1	35061
ATP2C1	224	IPI00024344.1	100576
ATP7A	106	IPI00028610.1	163335
ATP-binding cassette protein, sub-family B, member 1	104	IPI00027481.1	141463
ATP-binding cassette, sub-family A member 3	186	IPI00017800.1	191388
ATP-binding cassette, sub-family B, member 7	11	IPI00023879.1	82641
ATP-dependent metalloprotease FtsH1 homolog	105	IPI00045946.1	86503
Axonemal dynein heavy chain 8	26	IPI00014845.4	516063
BACE1	187	IPI00011518.1	55764
BAT1	27	IPI00218291.1	53243
Beta tubulin	307	IPI00142634.1	49671

BIG1	110	IP100002188.1	208709	
Brain-specific GTP-binding protein	225	IP100103530.1	63543	
BSCv protein (FRAGMENT)	188	IP100031131.1	46480	
BTAf1	111	IP100024802.1	206887	
C20orf11 (sim to a region of RANBPM)	28	IP100016634.1	26749	
Cadherin EGF LAG seven-pass G-type receptor 2	30	IP100015346.1	317453	
Calcium-binding protein P22	117	IP100218924.1	22456	
Calsyntenin-1	31	IP100007257.1	109793	
Calsyntenin-2	32	IP100005491.1	107020	
Calsyntenin-3	33	IP100156997.1	106098	
CAMK2D	297	IP100013787.1	56297	
CAMK4	189	IP100002921.1	51926	
Casein kinase II beta chain	190	IP100010865.1	24942	
Cathepsin B	191	IP100013478.1	37808	
Cation-chloride cotransporter-interacting protein	118	IP100024998.1	96171	
CD97	112	IP100012052.1	91941	
CDM_HUMAN	113	IP100019387.1	27860	
CDW92	226	IP100005068.2	73296	
Centromere/kinetochore protein ZW10 homolog	119	IP100011631.1	88829	
Cerebral protein 10	120	IP100018730.1	52118	

CGB0_HUMAN	29	IP100032827.1	14585
CGI-13	114	IP100008847.1	52917
CGI-51	115	IP100215921.1	57429
cholinergic receptor, nicotinic, alpha polypeptide 3	183	IP100007259.1	55637
Chondroitin sulfate proteoglycan 6	34	IP100023102.1	141542
CHRNA3	116	IP100027751.1	57310
Chromatin-specific transcription elongation factor FACT 140 kDa subunit	35	IP100026970.1	119914
CNTNAP1	227	IP100219249.1	164756
COPINE FAMILY MEMBER.	281	IP100173232.1	61891
Copine III	282	IP100024403.1	60131
DAAM1	121	IP100000705.1	124245
Dachshund 2	283	IP100065787.1	65323
DAPK1	122	IP100021250.1	160018
DC6 protein	36	IP100024620.1	11529
DCTN1	192	IP100011446.1	127404
Delta-1 catenin	284	IP100015202.1	104958
Delta-6 fatty acid desaturase	193	IP100003544.1	52259
Delta-like homolog	298	IP100009191.1	41143
Deoxyhypusine synthase	308	IP100026829.1	40971
Dihydrofolate reductase	229	IP100030357.1	28844
Dkfzp586c1924	37	IP100031064.1	21527



DNM1	228	IP100012033.1	97407
DOCK3	123	IP100217985.1	233103
Down syndrome critical region protein 2	124	IP100030770.1	32854
Dynactin 2	309	IP100013802.2	44231
Dynein light chain 2A	38	IP100023551.1	10922
Dynein light chain-A	39	IP100007675.1	56627
ECP-51	12	IP100009104.1	51157
ECSIT	125	IP100106506.1	49148
ELAVL3	40	IP100031552.2	39547
Endocytic receptor Endo180	233	IP100005707.3	166655
ENG	230	IP100017567.1	70578
ENG00000168820 (hypothetical protein with p-loop)	41	IP100151716.2	30772
ENSG00000144840	194	IP100102897.1	26308
ensp00000297280 (hypothetical protein with p-loop)	184	IP100182852.1	130960
Eukaryotic translation initiation factor 4A, isoform	42	IP100025491.1	46154
EXT2	231	IP100004047.1	82255
EXTL3	232	IP100015135.1	104749
FACL1	126	IP100013161.1	78348
FACL3	195	IP100031397.1	80346
FACL4	196	IP100029737.1	79188

Fe65	13	IP100010843.1	77244	
Fe65L1	292	IP100023841.1	81080	
Filamin, gamma	45	IP100165017.1	291151	
FLJ10773	291	IP100171198.1	52401	
FLJ13660	234	IP100100927.1	56921	
FLJ13910	43	IP100009707.1	43993	
FLJ13977	197	IP100025520.1	53482	
FLJ20342	127	IP100015713.1	65084	
FLJ20420	128	IP100015833.1	26152	
FLJ20481	198	IP100016418.1	47655	
FLJ22390	199	IP100009343.1	17098	
FLJ22555	129	IP100103303.1	32545	
FLJ22678	130	IP100217885.1	85495	
FRAP1	44	IP100031410.1	288892	
Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3	131	IP100014931.1	37062	
GAP-associated tyrosine phosphoprotein p62	14	IP100008575.1	48227	
GPR49	235	IP100021131.1	99998	
GTF2I	293	IP100054042.1	112416	
GTP-binding protein ERA	46	IP100026512.1	49098	
HADH2/ERAB (mitochondrial enzyme)	47	IP100017726.1	26923	

HDAC2	48	IP100023289.1	55325
HERC2 protein	49	IP100005826.1	527472
HK2	236	IP100005103.1	102368
homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)	219	IP100063544.1	33834
HSPC154	50	IP100107156.1	28202
HSPC245	51	IP100107104.1	26057
HTRA2	132	IP100001663.1	48841
HU-K4	133	IP100163951.1	48771
HU-K4	133	IP100163951.1	48771
Hunc18a	54	IP100046057.1	68736
HYPOTHEICAL PROTEIN	237	IP100164098.1	31105
Hypothetical protein (Fragment)	238	IP100161721.1	94945
HYPOTHEICAL PROTEIN FLJ10618	52	IP100018766.1	34095
Hypothetical protein FLJ10795	55	IP100024779.1	138430
HYPOTHEICAL PROTEIN FLJ12599.	53	IP100182757.1	102917
Hypothetical protein FLJ14562	239	IP100161141.1	67283
Hypothetical protein FLJ20397	56	IP100101654.1	26305
Hypothetical protein FLJ23356	135	IP100031005.1	40050
Hypothetical protein FLJ23630	240	IP100103520.1	73732
Hypothetical protein KIAA0372	241	IP100005634.1	175486

Hypothetical protein KIAA0455	136	IPi00160410.1	82983
Hypothetical protein KIAA0971-I	137	IPi00013735.1	81463
hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5	275	IPi00012235.1	24899
hypothetical protein MGC13186	98	IPi00031570.1	20713
hypothetical protein MGC22916	276	IPi00172590.1	88020
HYPOTHETICAL PROTEIN XP_174405.	134	IPi00159547.1	23035
ICAM-2	200	IPi00009477.1	30653
IGF2R	242	IPi00007226.1	274309
IKAP	57	IPi00028877.1	150191
IL13RA2	294	IPi00032199.1	44176
Insulinoma-glucagonoma protein 20	58	IPi00103536.1	183267
Integral membrane protein 2B (ITM2B)	16	IPi00031821.1	30338
Integral membrane transporter protein	277	IPi00020093.1	31735
IPi00104084.1	15	IPi00104084.1	36759
ITPR1	243	IPi00036162.1	313945
JIP-1	295	IPi00023133.1	77524
KIAA0056	59	IPi00000899.1	169718
KIAA0062 (FRAGMENT)	138	IPi00014236.1	58417
KIAA0090	139	IPi00160376.1	111759



KIAA0095	201	IP100005680.1	93488
KIAA0103	140	IP100014149.1	34833
KIAA0166	60	IP100001458.1	250749
KIAA0251 (FRAGMENT)	244	IP100010861.1	90027
KIAA0325 (FRAGMENT)	61	IP100141330.2	532367
KIAA0363 (FRAGMENT)	245	IP100004538.1	156999
KIAA0564	62	IP100158296.2	214824
KIAA0763	63	IP100006669.1	94914
KIAA0922	202	IP100021671.1	138688
KIAA0971	246	IP100007231.1	74536
KIAA1102 (Fragment)	285	IP100160387.1	121739
KIAA1181 (FRAGMENT)	203	IP100003635.1	36879
KIAA1250	247	IP100033429.1	197211
KIAA1533 (FRAGMENT)	204	IP100001841.1	72964
KIAA1949	299	IP100150950.1	67959
Krab box protein ensp00000302970	17	IP100154267.1	37912
Laminin, gamma 1	65	IP100003398.1	177607
LIB ( leucine-rich repeat protein)	64	IP100057018.2	64414
LRP5	248	IP100024531.1	179173
MBIP	66	IP100009868.1	39236
MEGF7 (FRAGMENT)	67	IP100023954.2	175609
MEP50	310	IP100012202.1	36724

Mesenchymal stem cell protein DSCD75	205	IP100010292.1	23865
MGC2803	286	IP100031526.1	18419
MGC4022	300	IP100010625.1	59797
MGC4248	141	IP100031582.1	24274
MGC5442	142	IP100027773.1	26261
MT-ACT48	68	IP100032410.1	46355
Myosin IXB	69	IP100003064.1	228624
NAP-1 related protein	301	IP100155244.1	44159
NEU1	70	IP100029817.1	45467
Neurexin-1	73	IP100006314.1	161883
Neurocalcin delta	302	IP100149712.1	22114
Neurotrypsin	206	IP100011063.1	97012
Nicestrin	147	IP100021983.1	78411
NICE-3	143	IP100032413.1	28779
NIPSNAP1	71	IP100021086.2	33310
NIPSNAP2	72	IP100016077.1	33743
NPC1	144	IP100005107.1	142149
NPD002	145	IP100152981.1	68760
NPL4, a component of the nuclear pore complex	146	IP100001676.1	73788
NRP2	249	IP100029693.1	104831

Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	311	IP100002922.2	55595
P63 protein	148	IP100141318.1	66022
Paladin	77	IP100161782.1	96754
PAS domain containing serine/threonine kinase	207	IP100141040.1	142859
PCDHA10	250	IP100001513.1	102875
PCDHB12	251	IP100001450.1	86770
PCDHB13: protocadherin beta 13	252	IP100001449.1	87552
Pcdhb17	258	IP100045942.1	64852
PCDHB4	253	IP100001429.1	87270
PCDHGB1	254	IP100003890.1	100360
PCDHGB6	255	IP100003897.1	101043
PDZ and LIM domain protein 1	74	IP100010414.2	36072
PDZ domain protein MAGI-3	18	IP100022491.1	111914
Pen-2	209	IP100020516.1	12029
Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	78	IP100004383.1	70637
PILB	75	IP100032871.1	21468
PILT	76	IP100010544.2	60705
PMPCB	256	IP100025726.1	54168
PP1, regulatory subunit 15B	208	IP100045837.1	79125
PP2C gamma	257	IP100006167.1	59272

PPP2CA (PP2A, catalytic subunit, alpha)	312	IPI00008380.1	35594
PPP2CB (PP2A, catalytic subunit, beta)	313	IPI00003461.1	35575
PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)	314	IPI00025326.1	65092
PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)	19	IPI00220836.1	55642
Presenilin-1	210	IPI00026333.1	52163
Presenilin-2	172	IPI00028485.1	50140
Procollagen C-endopeptidase enhancer	79	IPI00014828.1	47972
Programmed cell death 10	80	IPI00026997.1	24658
Prohibitin	173	IPI00017334.1	29804
Protein amplified in osteosarcoma (OS-9)	211	IPI00013268.1	75562
Protein similar to AGCP6688	81	IPI00140709.1	14290
Protein similar to probable mitotic centromere associated kinesin	20	IPI00088667.1	18400
Protein similar to stromal cell-derived factor 2	212	IPI00034198.1	23026
Protocadherin 7	259	IPI00001893.2	116105
Protocadherin beta 16	260	IPI00016595.1	84936
Protocadherin beta 8	213	IPI00009033.1	87624
PSMA1	149	IPI00016832.1	29556
PSMA3	150	IPI00016834.1	28302



PSMA4	151	IP100016836.1	29484	
PSMA6	152	IP100029623.1	27399	
PSMB1	153	IP100025019.1	26489	
PSMB2	154	IP100028006.1	22836	
PSMB3	155	IP100028004.2	22949	
PSMB4	156	IP100000806.1	29192	
PSMB5	157	IP100219629.1	28480	
PSMB6	158	IP100000811.2	25358	
PSMC1	159	IP100011126.2	49185	
PSMC2	160	IP100021435.1	48634	
PSMC3	161	IP100018398.2	49204	
PSMC4	162	IP100020042.2	47366	
PSMC5	163	IP100023919.2	45626	
PSMC6	164	IP100021926.2	44173	
PSMD1	165	IP100015333.1	105866	
PSMD11	166	IP100105598.1	47464	
PSMD12	167	IP100003569.1	52904	
PSMD13	168	IP100003570.1	42945	
PSMD2	169	IP100012268.1	100200	
PSMD3	170	IP100011603.2	60978	
PSMD4	171	IP100022694.1	40737	
RAB-18	261	IP100014577.1	22977	

Rab3 GTPase-activating protein, non-catalytic subunit	263	IP100018280.3	155985
RAB7L1			
RANBP1	82	IP100024775.1	23155
Reelin	83	IP100018856.1	23310
REP8 protein	85	IP100021018.1	388402
REST corepressor	214	IP100010353.1	30541
	303	IP100008531.1	53028
Retinal short-chain dehydrogenase/reductase retSDR2	216	IP100008260.1	32964
RING finger protein 5	215	IP100012608.1	19881
RNASEL	262	IP100015864.1	83533
RNB6	21	IP100008862.1	44792
RPGR-interacting protein 1	84	IP100044777.1	103123
RPS6KA3	174	IP100020898.1	83736
S-100 alpha	296	IP100010824.1	10415
S-100 beta	304	IP100220413.1	10713
SAP-62	22	IP100017341.2	49256
Serine/threonine protein phosphatase 6	90	IP100012970.1	35144
Sideroflexin 1	266	IP100009368.2	35619
Signal transducer and activator of transcription-1	267	IP100030781.1	87335
Similar to CGI-135 protein	268	IP100007052.1	16980

SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.	175	IP100058185.3	95055
similar to SD27354p [Drosophila melanogaster]	99	IP100103057.1	13291
SMAP-1B	264	IP100072534.1	103077
SNAP-25	86	IP100010470.1	23315
Sortilin 1	177	IP100016022.1	92100
Sortilin-related receptor	91	IP100022608.1	248441
SPTLC2	265	IP100005751.1	62924
Stearoyl-CoA desaturase	178	IP100100476.1	41523
Sterile alpha and HEAT/Armadillo motif protein	269	IP100007919.1	75337
Sterol O-acyltransferase 1	270	IP100019898.1	64763
STMN3	87	IP100021199.2	21017
STRA6 isoform 1	176	IP100154566.1	73533
Stromal cell-derived factor 2-like 1	217	IP100106642.2	23511
STX1A	88	IP100003370.1	33023
SUCLA2	89	IP100021996.2	50331
Synaptogyrin 3	92	IP100013947.1	24555
Tau	315	IP100025499.1	45850
tegt: testis enhanced gene transcript (bax inhibitor 1)	278	IP100022748.2	26538
Thioredoxin domain-containing protein	218	IP100001028.1	32535

TNRC15	287	IP100160501.1	127290
Tpar1	179	IP100102213.1	34906
TPST1	288	IP100030106.1	42188
Transcription factor CP2	23	IP100037599.1	57256
Triple functional domain protein (PTPRF interacting)	271	IP100026676.1	324106
TYK2	93	IP100022353.1	133660
tyrosine phosphatase ensg00000149185	220	IP100102935.1	22844
Ubiquitin-protein ligase E3-alpha	94	IP100156938.1	83595
Ubiquitin-protein ligase EDD	180	IP100026320.1	309352
UNC5C	272	IP100021472.1	103102
Vacuolar ATP synthase membrane sector associated protein m8-9	273	IP100041030.1	39036
vacuolar protein sorting protein 18	279	IP100060946.1	64959
VGF nerve growth factor inducible protein	95	IP100019628.1	67287
Voltage-dependent anion channel 2	181	IP100019625.1	31595
Wolframin	182	IP100008711.1	100306
X11beta	96	IP100017817.1	82512
X11beta	96	IP100017817.1	82512
Y391_HUMAN	274	IP100004584.1	65486
Zinc finger protein 198	97	IP100032608.2	154911
Zinc finger protein 277	24	IP100220069.1	56818



ZIP kinase	289	IPI00015213.1	52536
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TABLE 3

## BIOCHEMICAL ACTIVITIES OF THE COMPLEXES

Name of Complex	Biochemical activity
Fe65-complex	Regulator of APP processing and APP function
X11beta-complex	Regulator of APP processing and APP function
PSEN2-complex	Gamma-secretase complex
Nicastrin-complex	Gamma-secretase activity and assembly (trafficking)
Aph-1a-complex	Gamma-secretase activity and assembly (trafficking)
Pen-2-complex	Gamma-secretase activity and assembly (trafficking)
APP695SW-complex	Signalling activity (regulator of transcription)
APP-C99-complex	Signalling activity (regulator of transcription)
Tau-complex	Regulator of microtubules and vesicle transport along microtubules
APP695SW	Signalling activity (regulator of transcription)

TABLE 4

## MEDICAL APPLICATIONS OF THE COMPLEXES

Complex	Medical application
Fe65-complex	neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer
X11b-complex	neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arterosclerosis
PSEN2-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Nicastrin-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Aph-1a-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Pen-2-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
APP695SW-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
APP-C99-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Tau-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.



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## SEQID No:1

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## SEQID No:2

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SVFYYEILNSPEKACSLAKTAFDEAIAELDTLNEESYKDSTLIMQLLRDNLTWTSENQG  
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## SEQID No:3

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## SEQID No:5

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SEQID No:6

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SEQID No:8

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YDVYKSEFPTEADLEDFTAAVDEDEDEEEGEEVVEDRDYDYDTFKGDDYNEENPTE  
PGSDGTMSDKEITHDVKAVCSQEAMTGPCRAVMRWFYDLSKGGKCVRFIYGGCGGNR  
NNFESEDYCMVCKAMIPPTPLPTNDVDVYFETSADDNEHARFQKAKEQLEIRHRNRM  
DRVKKWEWEAELQAKNLPKAERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAM  
LNDRRRMALENYLAALQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKA

AQMKSQVMTHLHVIEERRNQSLSLLYKVPYVAQEIQEEIDELLQEQRADMDQFTASISE  
 TPVDVRVSSEEESEEIPPFHPPHPPALPENEDTQPELYHPMKKGGSGVGEQDGGGLIGAE  
 EKVINSKNKVDENMVIDETLDVKEMIFNAERVGGLEEERESVGPLREDFSLSSSALIGLL  
 VIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQRNHGYENPTYKYLEQ  
 MQI

## SEQID No:9

MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDS DPS  
 GTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR  
 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMMLPC  
 GIDKFRGVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEE  
 EEVAEEVEEEEADDDDEDEDGDEVEEEEAEOPYEEATERTTSIATTTTTTTTESVEEVREV  
 CSEQAETGPCRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMS  
 QSLLKTTQEPLARDPVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRER  
 MSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVE  
 AMLNDRRRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDP  
 KKAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDVLAN  
 MISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSV PANTENEVE  
 PVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS  
 NKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGY  
 ENPTYKFFEQMQN

## SEQID No:10

MDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSI  
 HHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

## SEQID No:11

MALLAMHSWRWAAAAAAFEKRRHSAILIRPLVSVSGSGPQWRPHQLGALGTARAYQIP  
 ESLKSITWQRLGKGNSGQFLDAAKALQVWPLIEKRTCWHGHAGGGGLHTDPKEGLKDV  
 DTRKIIKAMLSYVWPKDRPDLRARVAISLGFLGGAKAMNIVVPFMFKYAVDSL NQMSGN  
 MLNLSDAPNTVATMATAVLIGYGVS RAGAAFFNEVRNAVFGKVAQNSIRRIAKNVFLHL  
 HNLDLGFHLSRQTGALS KAIDRGTRGISFVLSALVFNLLPIMFEVMLVSGVLYYKCGAQF  
 ALVTLGTLGTYTAFTVAVTRWRTRFRIEMNKADNDAGNAIDSLLNYETVKYFN NERYE  
 AQRDYGFLKTYETASLKSTSTLAMLNFGQSAIFSVGLTAIMVLASQGIVAGTLTVGDLVM



VNGLLFQLSLPLNFLGTVYRETRQALIDMNTLFTLLKVDTQIKDKVMASPLQITPQTATVA  
 FDNVHFEYIEGQKVLSGISFEVPAGKKVAIVGGSGSGKSTIVRLLFRFYEPQKGSYLAG  
 QNIQDVSLESLRRAVGVVPQDAVLFHNTIYYNLLYGNISASPEEVYAVAKLAGLHDAILR  
 MPHGYDTQVGERGLKLSGGEKQRVAIARAILKDPPVILYDEATSSLD SITEETILGAMKD  
 VVKHRTSIFIAHRLSTVVDADIIVLDQGKVAERGTHHGLLANPHSIYSEMWHTQSSRVQ  
 NHDNPKWEAKKENISKEEERKKLQEEIVNSVKGCGNCSC

SEQID No:12

MATVTATTKVPEIRDVTRIERIGAHSHIRGLGLDDALEPRQASQGMVGQLAARRAAGVV  
 LEMIREGKIAGRAVLIAGQPGTGKTAIAMGMAQALGPDTPFTAIAGSEIFSLEMSKTEALT  
 QAFRRSIGVRIKEETEIIIEGEVVEIQIDRPATGTGSKVGKLTTLKTTEMETIYDLGTKMIESL  
 TKDKVQAGDVITIDKATGKISKLGSRFTRARDYDAMGSQTKFVQCPDGELQKRKEVVHT  
 VSLHEIDVINSRTQGFLALFSGDTGEIKSEVREQINAKVAEWREEGKAEIIPGVLFIDEVH  
 MLDIESFSFLNRALES DMAPVLIMATNRGITRIRGTSYQSPHGIPIDLLDRLLIVSTTPYSE  
 KDTKQILRIRCEEEDVEMSEDAYTVLTRIGLETSLRYAIQLITAASLVCRKRKGTEVQVDD  
 IKRVYSLFLDESIRSTQYMKEYQDAFLFNELKGETMDTS

SEQID No:13

MSVPSSLSQSAINANSHGGPALSPLPLHAAHNQLLNAKLQATAVGPKDLRSAMGEGG  
 GPEPGPANAKWLKEGQNQLRRAATAHRDQNRNVTLTAAEEASQEP EMAPLGPKGLIHL  
 YSELELSAHNAANRGLRGPGLIISTQE QGPDEGE EKAAGEAEEEEEDDDDEEEEEEDLS  
 SPPGLPEPLESVEAPPRPQALTDGPREHSKSASLLFGMRNSAASDEDSSWATLSQGSP  
 SYGSPEDTDSFWNPNAFETDSDL PAGWMRVQDTSGTYYYWHIPTGTTQWEPPGRASP  
 SQGSSPQEESQLTWTGFAHGEGFEDGEFWKDEPSDEAPMELGLKEPEEGTLTFPAQS  
 LSPEPLPQEEEEKLPPRNTNPGIKCFAVRSLGWVEMTEEELAPGRSSVAVNNCIRQLSYH  
 KNNLHDPMSGGWGEGKDLLLQLEDETLKLVEPQSQALLHAQPIISIRVWGVGRDSGRE  
 RDFAYVARDKLTQMLKCHVFRCEAPAKNIATSLHEICKSKIMAERRNARCLVNGLSLDHS  
 KLVDVPFQVEFPAPKNELVQKFQVYYLGNVPVAKPVGVDVINGALESVLSSSSSREQWT  
 PSHVSVAPATLTILHQQTEAVLGECRVRFLSFLAVGRDVHTFAFIMAAGPASFCCHMFW  
 CEPNAASLSEAVQAACMLRYQKCLDARSQASTSCLPAPPAESVARRVGWTVRRGVQS  
 LWGSLKPKRLGAHTP

SEQID No:14

MQRRDDPAARMSRSSGRSGSMDPSGAHPSVRQTPSRQPPLPHRSRGGGGGGSRGGA

RASPATQPPPLLPPSATGPDATVGGPAPTPLLPPSATASVKMEPENKYLPELMAEKDSL  
DPSFTHAMQLLTAEIEKIQKGDSKKDDEENYLDLFSHKNMKLKERVLPVKQYPKFNFVG  
KILGPQGNTIKRLQEETGAKISVLGKGSMRDKAKEEELRKGGDPKYAHLNMDLHVFEV  
FGPPCEAYALMAHAMEEVKKFLVPDMMDDICQEQFLELSYLVPEPSRGRGVVVRG  
RGAAPPPPPVPRGRGVGPPRGALVRGTPVRGAITRGATVTRGVPPPPTVRGAPAPRA  
RTAGIQRIPLPPPPAPETYEEYGYDDTYAEQSYEGYEGYYSQSQGDSEYYDYGHGEVQ  
DSYEAYGQDDWNGTRPSLKAPPARPVKGAYREHPYGRY

SEQID No:15

ISALQKGYSKVLCQTLSEARNSEITSLKNEGENLKRDNATSGMVSSLQKDILAKDEQVQQ  
LKEEVSHLKSQNKDKDHQLEALGSRCVSLKEELKQEDAHRELREAEKEKELCKTVEE  
KLQEDSRRKLLQLQEMGNRESVIKINLERAVGQLEHFRSQVIKATYGRAKPFRDKPVT  
DQQLIEKITQVTEDNINFQQKKWTLQKETQLSNSKQEETTENIEKLRTSLDSCQACMKISC  
CSHDLKKEVDLLQHLQVSPPVSGLQKVVLDRHALSWLEEVEQLLRDLGILPSSPNKG  
FSLYLIYLLEHYKKLMSQAQELQ

SEQID No:16

MVKVTFNSALAQKEAKKDEPKSGEEALIIPDAVAVDCKDPDDVVPVGQRRRAWCWC  
MCFGALFMLAGVILGGAYLYKYFALQPDDVYYCGIKYIKDDVILNEPSADAPAALYQTIE  
ENIKIFEEEEVEFISVPVPEFADSDPANIVHDFNKKLTAYLDLNDKCYVIPLNTSIVMP  
PRNLLELLINIKAGTYLPQSYLIHEHMTDRIENIDHLGFFIYRLCHDKETYKLQRRET  
IKGIQKREASNCFAIRHFENKFAVETLICS

SEQID No:17

MASRPRPRTPSRGPSDLRFRGEAGLRRVFLKKAGVRVRPADKRAAGSRVGCPWHRA  
EPPLGTREQQGFRKRERRWTGGRPGFAQAPPLGGPAQGALRQFPCDVAVGFTQEEW  
QHLDQAQRTPYRDMMLLENYSLLLSVGYCITKPEVVCKLEHGQVLWILEEESPSQSHLDC  
CIDDDLMEKRQENQDQHLQKVDFVNNKTLTMDRNGVLGKTFSLDTNPILSRKIRGNCD  
SSGMNLNNISELIISNRSSFVRNPAECNVRGKFLLCMKRENPYARGKPLEYDGNGKAVS  
QNEDLFRHQYIQTLKQCFEYNQCGKAFHEEAACSTHKRVCSWETL

SEQID No:18

DVIVDINGNCVLGHTHADVVQMFQLVPVNQYVNLTLCRGYPLPDDSEDPVVDIVAATPVI  
NGQSLTKGETCMNPQDFKPGAMVLEQNGKSGHTLTGDGLNGPSDASEQRVSMASG

SSQPELVTIPLIKGPKGFGFAIADSPTGQKVKMILDSQWCQGLQKGDIIKEIYHQNVQNL  
 HLQVVEVLKQFPVGADVPLLILRGGPPSPTKTAKMKTDKKENAGSLEAINEPIQPMPFP  
 PSIIRSGSPKLDPSEVYLKSKTLYEDKPPNTKDLDVFLRKQESGFGFRVLGGDGPDQSIY  
 IGAIPLGAAEKDGRRLRAADELMCIDGIPVKGKSHKQVLDLMTTAARNGHVLLTVRRKIFY  
 GEKQPEDDSSQAFISTQNGSPRLNRAEVPARPAQEPYDVVLQRKENEGFGFVILTSK  
 NKPPPGVIPHKIGRVIEGSPADRCGKLKVGDDHISAVNGQSIVELSHDNIVQLIKDAGVTVT  
 LTVIAEEEEHHGPPSGTNSARQSPALQHRPMGQSQANHIPGDRSALEGEIGKDVSTSYR  
 HSWSDHKHLAQPD TAVISVVGSRHNQNLGCYPVELERGPRGFGFSLRGGKEYNMGLF  
 ILRLAEDGPAIKDGRIHVGDQIVEINGEPTQGITHTRAIELIQAGGNKVLLLLLRPGTGLIPD  
 HGDWDINNPSSSNVIYDEQSPLPPSSHFA SIFEESHVPVIEESLRVQICEKAEELKDIVPE  
 KKSTLNENQPEIKHQ SLLQKNVSKRDPSSHGHHSNKKNLLKVENGVTTRGRSVSPKKP  
 ASQHSEEHLDKIPSPLKNNPKRRPRDQSLSPSKGENKSCQVSTRAGSGQDQCRKSRG  
 RSASPKKQQKIEGSKAPSNAEAKLLEGKSRRIAGYTGSNAEQIPDGKEKSDVIRKDAKQ  
 NQLEKSRTSPEKKIKRMVEKSLPSKMTNKTTSKEVSENEKGKKVTTGETSSSNDKIGE  
 NVQLSEKRLKQEPEEKVVS NKTEDHKGKELEAADKNKETGRFKPESSSPVKKTLITPGP  
 WKVPSGNKVTGTIGMAEK RQ

SEQID No:19

HPPPSALSTPPSPGEGGEFRKRRPRGTQQGHHLQRNMAGAGGGNDIQWCFSQVKGA  
 VDDDVAEADIISTVEFNHSGELLATGDKGGRVVIFQQEQENKIQSHSRGEYNVYSTFQS  
 HEPEFDYLSLEIEEKINKIRWLPQKNAAQFLLSTNDKTIKLWKISERDKRPEGYNLKEED  
 GRYRDPTTVTTLRVPVFRPMDLMVEASPRRIFANAHTYHINSISINSYETYSADDLRIN  
 LWHLEITDRSFNIVDIKPANMEELTEVITAAEFHPNSCNTFVYSSSKGTIRLCDMRASALC  
 DRHSLKFEEPEDPSNRSFFSEIISISDVKFSSHSGRYMMTRDYLSVKIWDNLNMENRPVE  
 TYQVHEYLRSLKCSLYENDCIFDKFECCWNGSDSVVMTGSYNNFFRMFDRNTKRDITL  
 EASRENNKPRTVLKPRKVCASGKRKKDEISVDSLDFNKKILHTAWHPKENIIAVATTNNL  
 YIFQDKVN

SEQID No:20

MEKIRVCVRKRPLGMREVRRGEINIITVEDKETLLVHEKKEAVDLTQYILQHVIFYFDEVF  
 GEACTNQDVYMKTTTHPLIQHIFNGGNATCFAYGQTGAGKTYTMIGTHENPGLYALAAK  
 DIFRQLEVSQPRKHLFWWISFYEIYCGQLYDLLNRRKRY

SEQID No:21

MATSEQSICQARASVMVYDDTSKKWVPIKPGQQGFSRINIYHNTASNTFRVVGVLQD  
 QQVVINYSIVKGLKYNQATPTFHQWRDARQVYGLNFASKEEATTFSNAMLFALNIMNSQ  
 EGGPSSQRQVQNGPSPDEMDIQRRQVMEQHQQQRQESLERRTSATGPILPPGHPSS  
 AASAPVSCSGPPPPPPPPVPPPPTGATPPPPPPPLPAGGAQGSSHDESSMSGGLAAAIAG  
 AKLRRVQRPEDASGGSSPSGTSKSDANRASSGGGGGGGLMEEMNKLLAKRRKAASQS  
 DKPAEKKEDESQMEDPSTSPSPGTRAASQPPNSSEAGRKPWERSNSVEKPVSSILSRT  
 PSVAKSPEAKSPLQSQPHSRMKPAGSVNDMALDAFDLDRMKQEILEEVVRELHKVKEE  
 IIDAIRQEELSGISTT

SEQID No:22

MDFQHRPGGKTGSGGVASSSESNRDRRERLRQLALETIDINKDPYFMKNHLGSECKL  
 CLTLHNNEGSYLAHTQGKKHQTNLARRAAKEAKEAPAQPAPEKVKVEVKKFVKIGRPG  
 YKVTQKRDSEMGQQSLLFQIDYPEIAEGIMPRHRFMSAYEQRIEPPDRRWQYLLMAAE  
 PYETIAFKVPSREIDKAEGKFWTHWNRETKQFFLQFHFMEKPPAPPSLPAGPPGVKR  
 PPPPLMNGLP RPPLPESLPPPPPGGLPLPPMPPTGPAPSGPPGPPQLPPPAPGVHPP  
 APVVHPPASGVHPPAPGVHPPAPGVHPPAPGVHPPTSGVHPPAPGVHPPAPGVHPPA  
 PGVHPPAPGVHPPAPGVHPPPSAGVHPQAPGVHPAAPAVHPQAPGVHPPAPGMHPQ  
 APGVHPQPPGVHPSAPGVHPQPPGVHPSNPGVHPPTPMPPMLRPPLPSEGPGNIPPP  
 PPTN

SEQID No:23

MAWALKLPLADEVIESGLVQDFDASLSGIGQELGAGAYSMSDVLALPIFKQEESLPPD  
 NENKILPFQYVLCAATSPAVKLHDETLYLNQGQSYEIRMLDNRKLGELPEINGKLVKSIF  
 RVVFHDRRLQYTEHQQLEGWRWRNRP GDRILDIDIPMSVGIIDPRANPTQLNTVEFLWDP  
 AKRTSVFIQVHCISTEFTMRKHGGEKGV PFRVQIDTFKENENGEYTEHLHSASCQIKVFK  
 PKGADRKQKTDREKMEKRTPHEKEKYQPSYETITLTCSPWPEITYVNNSPSPGFNSS  
 HSSFSLGEGNGSPNHQPEPPPPVTDNLLPTTTPQEAQQWLHRNRFSTFTRLFTNFSGA  
 DLLKLTRDDVIQICGPADGIRLFNALKGRMVRPRLTIYVCQESLQLREQQQQQQQQQK  
 HEDGDSNGTFFVYHAIYLEELTAVELTEKIAQLFSISPCQISQIYKQGPTGIHVLISDEMIQ  
 NFQEEACFILD TMKAETNDSYHIILK

SEQID No:24

VWRKHVVDGEFASSSVSTGATPPPTRPAALPFLFCRVMAASKTQGAVARMQEDRDGS



CSTVGGVGYGDSKDCILEPLSLPESPGGTTTLEGSPSVPCIFCEEHFPVAEQDKLLKHHMI  
 IEHKIVIADVCLVADFQRYILYWRKRFTREQPITDFCSVIRINSTAPFEEQENYFLLCDVLPE  
 DRILREELQKQRLREILEQQQQERNDTNFHGVCMFCNEEFLGNRSVILNHMAREHAFNI  
 GLPDNIVNCNEFLCTLQKKLDNLQCLYCEKTFRDKNTLKDHRMRKKQHRKINPKNREYDR  
 FYVINYLELGKSWEEVQLEDDRELLDHQEDDWSDEEHPASAVCLFCEKQAETIEKLY  
 VHMEDAHEFDLLKIKSELGLNFYQQVKLVNFIRRVHQCRCYGGCHVKFKSKADLRTHM  
 EETKHTSLLPDRKTWDQLEYFYPTYENDTLLCTLSDSESDLTAEQENENVPIISEDTSKL  
 YALKQSSILNQLLL

SEQID No:25

MRLTHICCCCLLYQLGFLSNGIVSELQFAPDREEWEVVPALWRREPVDPAAGGSGGSA  
 DPGWVRGVGGGGGSARAQAAGSSREVRVAPVPLEEPVEGRSESRLRPPPPSEGEED  
 EELESQELPRGSSGAAALSPGAPASWQPPPPPPQPPPSPPPAQHAEPDGDEVLLRIPAF  
 SRDLYLLLRRDGRFLAPRFAVEQRPNP GPGPTGAASAPQPPAPPDAGCFYTGAVLRHP  
 GSLASFSTCGGGLMGFIQLNEDFIFIEPLNDTMAITGHPHRVYRQKRSMEEKVTEKSAL  
 HSHYCGIISDKGRPRSRKIAESGRGKRYSYKLPQEYNIETVVVADPAMVSYHGADAARR  
 FILTILNMVFNLFQHKSLGVQVNLRVIKLILLHETPPELYIGHHGEKMLESFCKWQHEEFG  
 KKNDIHLEMSTNWGEDMTSVDAILITRKDFCVHKDEPCDTVGIAYLSGMCSEKRKCIIA  
 EDNGLNLAFTIAHEMGMHNMGINHDNDHPSCADGLHIMSGEWIKGQNLGDVSWSRCSEK  
 EDLERFLRSKASNCLLQTNPQSVNSVMVPSKLPGMTYTADEQCQILFGPLASFCQEMQ  
 HVICTGLWCKVEGEKECRTKLDPMDGTDCLGKWCKAGECTSRSAPEHLAGEWSL  
 WSPCSRTCSAGISSRERKCPGLDSEARDCNGPRKQYRICENPPCPAGLPGRDWQCQ  
 AYSVRTSSPKHILQWQAVLDEEKPCALFCSPVGKEQPILLSEKVMGTSCGYQGLDICA  
 NGRCQKVGCDGLLGLSLAREDHCGVCNGNGKSKKIKGDFNHTRGAGYVEVLVIPAGAR  
 RIKVVEEKPAHSYLALRDAGKQSINSDWKIEHSGAFNLAGTTVHYVRRGLWEKISAKGP  
 TTAPLHLLVLLFQDQNYGLHYEYTIPTSDPLPENQSSKAPEPLFMWTHTSWEDCDATCG  
 GGERKTTVSCTKIMSKNISIVDNEKCKYLTKEPEQIRKCNQPCQTRWMMTEWTPCSR  
 TCGKGMQSRQVACTQQLSNGTLIRARERDCIGPKPASAQRCQDCMTVWEAGVWS  
 EFSVKCGKGIRHRTVRCTNPRKKCVLSTRPREAEDCEDYSKCYVWRMGDWSKCSITC  
 GKGMQSRVIQCMHKITGRHGNECFSSSEKPAAYRPCHLQPCNEKINVNTITSPRLAALTF  
 KCLGDQWPVYCRVIREKNLCQDMRWYQRCCECTCRDFYAQKLQOKS

SEQID No:26

MMKLYIDNAAPDKLKGLCFFVRCRNDVAINVKTIQEEALFTVLDASKGLLNGIRDMLANI

FLPAVLATNNWGALNQSKQGESEKHIFTETINRYLSFLDGARISIEGTVKLKTIDNVNFSK  
LHTFEEVTAAASNSETVHQLEEVLMVWYKQIEQVLIIESEQMRKEAGDSGPLTELEHWK  
RMSAKFNYIIEQIKGPSCKAVINVLNVAHASKLLKNWRDLARITDTANESKDNVRYLYTLE  
KVCQPLYNHDLVSMAGIQNLINAIRMIHGVSRYNTSERMTSLFIKVTNQMV TACKAYI  
TDGGLNHVWDQETPVVLKKIQDCIFLFKEYQASFHKTRKLISESSGEKSFEVSEMYIFGK  
FEAFCKRLEKITEMITVVQTYSTLSNSTIEGIDIMAIKFRNIYQGVKKKQYDILDPRRTEFD  
TDFLDFMTKINGLEVQIQAFMNSSFGKILSSQQALQLLQRFQKLNIPCLGLEINHTIERILQ  
YYVAELDATKKASLYHSQKDDPPLARNMPPIAGKILWVRQLYRRRISEPINYFFKNSDILSS  
PDGKAVIRQYNKISYVLVEFEVVYHTAWIREISQLHYALQATLFVRHPETGKLLVNFDPKI  
LEV VRET KCMIKMKLDVPEQAKRLLKLESKLLKADKLYLQGLLQYYDEL CQEVPSVFNL  
MTPKMKKVESVLRQGLTVLTWSSLTLESFFQEVELVLD MFNQLLKKISDLCEMHIDTVLK  
EIAKTVLISLPESGATKVEDMLTLNETYTKEWADILNHKSKHVEEAVRELISIFEQIYEVKY  
TGKVGKQSEQQRKHVVFGSETGEGENNDYEANIVNEFDTHDKEDEFKKECKEVFAFFSH  
QLLDSLQKATRLSLDTMKRRIFVARQVENMLIILYGRKQSEDIISFIKSEVHLAIPNVVMIP  
SLDDIQQAINRMIQLTLEVSRGVAHWGQQQIRPIKSVIPSPTTTDVTHQNTGKLLKKEER  
SFEEAIPARKLKNFYPGVAEHKDISKLVL LSSSVNSLRKAAHEALQDFQKYKTLWTEDR  
DVKVKEFLANNPSLTEIRSEILHYATFEQEIDELKPIIVGAELEHTEPMKLALSIEAKAWK  
MLLCRYLNEEYKKKMSYMI AFINEYLKKLSRPIRDLD D VRFAMEALSCIRDNEIQMDMTL  
GPIEEAYAILNRFEVEVTKEESEAVDTLRYSFNKLQSKAVSVQEDLVQVQPKFKSNLLES  
VEVFREDVINFAEAYELEGPMVPNIPPQEASNRLQIFQASFDDLWRKFVTYSSGEQLFG  
LPVTDYEVLHKTRKELNLLQKLYGLYDTVMSSISGYYEILWGDVDIEKINAEELLE FQNR  
RKLPKGLKDWQAFLDLKKRIDDFSESCPLLEMMTNKAMKQRHWDRISELTGTPFDVES  
DSFCLRNIMEAPLLKHKDDIEDICISAIKEKDIEAKLTQVIENWTNQNL SFAAFKGKGELL  
KGTESGEIITLMEDSLMVLGSLLSNRYNAPFKKNIQNWVYKLSTSSDIIEEWLVVQNLWV  
YLEAVFVG GDI AKQLPQEAKRFQNI DKSWIKIMQRAHENPNVINCCV GDET MGQLLPHL  
HEQLEVCQKSLTGYLEKKRLLFPRFFFVSDPV LLEILGQASDSHTIQPHLPAVSDNINEVT  
FHA KDYDRIMAVISREGEKIVLDNSVMAKGPVEIWLLDLLKMQMSSLHNIIRSAFYQISDS  
GFQLLPFLSHFPAQVGLLGIQMLWTHDSEEALRNAKDDR KIMQVTNQKFLDILNTLISQT  
THDLSKFDRVKFETLITIHVHQRDIFDDL VKMHIKSPTDFEWL KQSRFYFKEDLDQTVVSI  
TDVDFIYQNEFLGCTDRLVITPLTDRCYITLAQALGMNMGGAPAGPAGTGKTETTKDMG  
RCLGKYVVVFNCSDQMDFRGLGRIFKGKCLAQSGSWGCFDEFNRIELPVLSVAAQQIYI  
VLTARKERKKQFIFSDGDCVDLNPEFGIFLTMPGYAGRQELPENLKI QFRTVAMMVPD  
RQIIMRVKLASCGFLENVILAQKFYVLYKLCEEQLTKQVHYDFGLRNILSVLRTLGSQKRA  
RPEDSELSIVMRGLRDMNLSKLVDEDEPLFLSLINDLFPGLQLDSNTYAELQNAVAHQV

QIEGLINHPPWNLKLVQLYETSLVRHGLMTLGPSSGSKTTVITILMKAQTECGRPHREM  
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 NSVLDDNKTLTLANGDRIPMAPSCKLLFEVHNIENASPATVSRMGMMVYISSSALSWRPIL  
 QAWLKKRTAQEA AVFLTLYEKFVEDTYTYMKLNLNPKMQLLECNYIVQSLNLLEGLIPSK  
 EEGGVSCVEHLHKLFVFGMLMWSLGALLELESREKLEAFLRQHESKLDLPEIPKGSNQTM  
 YEFYVTDYGDWEHWNKKLQPYYYPTDSIPEYSSILVPNVDNIRTNFLIDTIAKQHKAVLLT  
 GEQGTAKTVMVKAYLK KYDPEVQLSKSLNFSSATEPMMFQRTIESYVDKRIGSTYGPP  
 GGRKMTVFIDDINMPVINEWGDQITNEIVRQMMEMEGMYSLDKPGDFTTIVDVQLIAAMI  
 HPGGGRNDIPQRLKRQFTVFNCTLPSNASIDKIFGIIGCGYFDPCRSFKPQICEMIVNLVS  
 VGRVLWQWTKVKMLPTPSKFHYIFNLRLDLSRIWQGM LTIKAEECASIPTLLSLFKHECSR  
 VIADR FITPEDEQWFNAHLTRAVEENIGSDAASCILPEPYFVD FLREMPEPTGDEPEDSV  
 FEVPKIYELMPSFD FLAEKLQFYQRQFNEIIRGTSLDLVFFKDAMTHLIKISRIIRTSCGNA  
 LLVGVGSGSGKQSL SRLASFIAGYQIFQITLRSYNVTNL TDDLKALYKVAGADGKGITFIF  
 TDSEIKDEAFLEYLNNLLSSGEISNLFARDEMDEITQGLISVMKRELPRHPPTFDNLYEYF  
 ISRSRKNLHVLCFSPVGEKFRARSLKFPGLISGCTMDWFSRWPREALIAVASYFLSDY  
 NIVCSSEIKRQVVETMGLFHD MVSESCESYFQRYRRRAHVTPKSYLSFINGYKNIYAEK  
 VKFINEQAERMNIGLDKLMEASESVAKLSQDLAVKEKELAVASIKADEVLAEVTVSAQAS  
 AKIKNEVQEVKDKAQKIVDEIDSEKVKAESKLEAAKPALEEAEAA LNTIKPNDIATVRKLA  
 KPPHLIMRIMDCVLLL FQKKIDPVTMDPEKSCCKPSWGESLKLMSATGFLWSLQQFPKD  
 TINEETVELLQPYFNMDDYTFESA KKVCGNVAGLLSWTLAMAIFYGINREVLPLKANLAK  
 QEGR LAVANAELGKAQALLDEKQAELDKVQAKFDAAMNEKMDLLNDADTCRKKMQAA  
 STLIDGLSGEKIRWTQQSKEFKAQINRLVGDILLCTGFLSYLGPFNQIFRNYLLKDQWEM  
 ELRARKIPFTENLNLISMLVDPPTIGEWGLQGLPGDDLSIQNGIIVTKATRYPLLIDPQTQG  
 KTWIKSKEKENDLQVTSLNHKYFRTHLED SLSLGRPLLIEDIHEELDPA LDNVLEKNFIKS  
 GTTFKVKGDK ECDIMDTFKLYITTKLPNPAFTPEINAKTSVIDFTVTMKGLENQLLRRVIL  
 TEKQELEAERVKLLEDVTFNKRKMKELEDNLLYKLSATKGSLVDDES LIGVLRTTKQTAA  
 EVSEKLHVAAETEIKINAAQEEFRPAATRGSILYFLITEMSMVNIMYQTS LAQFLKLFDQS  
 MARSEKSPLPQKRITNII EYLT YE VFTYSVRGLYENHKFLFVLLMTLKIDLQRGTVKHREF  
 QALIKGGAALDLKACPPKPYRWILD MTWLN LVELSKLPQFAEIMNQISRNEKGWKS WFD  
 KDAPEEEIIPDGYNDSLDTCHKLLLIRSWCPDRTVFQARKYIADSLEEKYTEPVILNLEKT  
 WEESDTRTPLICFLSMGSDPTNQIDALAKKLE CRTISMGGQGEVHARKLIQMSMQQ  
 GGWVLLQNCHLGLEFMEELLETLITTEASDD SFRVWITTEPHDRFPITLLQTS LKFTNEP  
 PQGVRAGLKRTFAGINQDLLDISNLP MWKPMLYTVAF LHSTVQERRKFGPLGWNIPYEF  
 NSADFSASVQFIQNH LDEC DIKKGVS WNTVRYMIGEVQYGGRV TDDFDKRL LNCFARV



WFSEKMFEPSFCFYTGKIPCKTLDQYFEYIQSLPSLDNPEVFGLHPNADITYQSNTAS  
 AVLETITNIQPKESGGGVGETREAIYRLSEDMLSKLPPDYIPHEVKSRLIKMGHLNSMNI  
 FLRQEIDRMQRVISILRSSLSDLKLAIEGTIIMSENLRDALDNMYDARIPQLWKRVSWDSS  
 TLGFWFTELLERNAQFSTWIFEGRPNVFWMTGFFNPQGFLTAMRQEVTRAHKGWALD  
 TVTIHNEVLRQTKEEITSPPGEGVYIYGLYMDGAAWDRRNGKLMESTPKVLFTQLPVLHI  
 FAINSTAPKDPKLYVCPIYKKPRRTDLTFITVVYLRTVLSPDHWILRGVALLCDIK

SEQID No:27

YLCFPLLFLNPLLFTPCFHLFCENPSRSPFPSSPAGPVMAENDVDNELLDYEDDEVETA  
 AGGDGAEAPAKKDVKGSYVSIHSSGFRDFLLKPELLRAIVDCGFEHPSEVQHECIPQAIL  
 GMDVLCQAKSGMGKTAVFVLATLQQLEPVTGQVSVLVMCHTRELAFQISKEYERFSKY  
 MPNVKVAVFFGGLSIKKDEEVLLKKNCPHIVVGTPGRILALARNKSLNLKHIKHFILDECDK  
 MLEQLDMRRDVQEIFRMTPEHKQVMMFSATLSKEIRPVCRKFMQDPMEIFVDDDETCLT  
 LHGLQQYYVKLKDNEKNRKLFDLLDVLEFNQVVIFVKSVQRCIALAQLLVEQNFPAAIAHR  
 GMPQEERLSRYQQFKDFQRRILVATNLFGRGMDIERVNIAFNYPEDSDTYLHRVAR  
 AGRFGTKGLAITFVSDENDAKILNDVQDRFEVNISELPDEIDISSYIEQTR

SEQID No:28

MSYAEKPDEITKDEWMEKLNHLHVQRADMNRLIMNYLVTEGFKEAAEKFRMESGIEPS  
 VDLETLDERIKIREMILKGQIQEAIALINSLHPELLDTNRYLYFHLQQQHLELIRQRETEAA  
 LEFAQTQLAEQGEESRECLTEMERTLALLAFDSPEESPFGDLLHTMQRQKQVWSEVNQA  
 VLDYENRESTPKLAKLLKLLLWAQNELDQKKVKYPKMTDLSKGVIEEPK

SEQID No:29

MAMQAAKRANIRLPPEVNRILYIRNLPYKITAEEMYDIFGKYGPIRQIRVGNTPETRGTA  
 VVYEDIFDAKNACDHLSGFNVCNRYLVVLYYNANRAFAQKMDTKKKEEQLKLLKEYGIN  
 TDPPK

SEQID No:30

MRSPATGVPLPTPPPLLLLLLLLLLPPPLLGDQVGPCRSLSRGRGSSGACAPMGWLC  
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 LLGIGGHLSPQGKLTLP EEHPCLKAPRLRCQSCKLAQAPGLRAGERSPEESLGGRKR  
 NVNTAPQFQPPSYQATVPENQPAGTPVASLRAIDPDEGEAGRLEYTMDALFDSRSNQF  
 FSLDPVTGAVTTAEELDRETKSTHVFRVTAQDHGMPRRSALATLTILVTDNDHDPVFE



QQEYKESLRENLEVGYEVLTVRATDGDAPPNANILYRLLEGSGGSPSEVFEIDPRSGVI  
 RTRGPVDREEVESYQLTVEASDQGRDPGPRSTTA AVFLSVEDDNDNAPQFSEKRYVV  
 QVREDVTPGAPVLRVTASDRDKGSNAVHYSIMSGNARGQFYLDAQTGALDVVSPLDY  
 ETTKEYTLRVRAQDGGRPPLSNVSGLVTQVLDINDNAPIFVSTPFQATVLESVPLGYLV  
 LHVQAIDADAGDNARLEYRLAGVGHDFPFTINNGTGWISVAAELDREEVDFYSFGVEAR  
 DHGTPALTASASVSVTVLDVNDNNPTFTQPEYTVRLNEDAAVGTSVVTVSAVDRDAHS  
 VITYQITSGNTRNRFSITSQSGGGLVSLALPLDYKLERQYVLAVTASDGTRQDTAQIVVN  
 VTDANTHRPVFQSSHYTVNVNEDRPAGTTVVLISATDEDTGENARITYFMEDSIPQFRID  
 ADTGAVTTQAELDYEDQVSYTLAITARDNGIPQKSDTTYLEILVNDVNDNAPQFLRDSYQ  
 GSVYEDVPPFTSVLQISATDRDSGLNGRVFYTFQGGDDGDGDFIVESTSGIVRTLRRLD  
 RENVAQYVLRAYAVDKGMPPARTPMEVTVTVLDVNDNPPVFEQDEFDVFVEENSPIGL  
 AVARVTATDPDEGTNAQIMYQIVEGNIPEVFQLDIFSGELTALVDLDYEDRPEYVLVIQAT  
 SAPLVS RATVHVRLDRNDNPPVLGNFEILFN NYVTNRSSSFPGGAIGRVP AHDPDISD  
 SLTYSFERGNELSLVLLNASTGELKLSRALDNNRPLEAIMSVLVSDGVH SVTAQCALRVT  
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 ILNVSLSVGQPPGPGGGPPFLPSEDLQERLYLNRSLT AISAQRVLPFDDNICLREPCEN  
 YMRCVSVLRFDSSAPFIASSSVLFRPIHPVGGLRCRCPPGFTGDYCE TEVDLCYSRPCG  
 PHGRCRSREGGYTCLCRDGYTGEHCEVSARSGRCTPGVCKNGGTCVNLLVGGFKCD  
 CPSGDFEKPYPYCQVTTRSFP AHSFITFRGLRQRFHFTLALS FATKERDGLLLYNGRFNEK  
 HDFVALEVIQEQVQLTFSAGESTTTVSPFVPGGVSDGQWHTVQLKYYNKPLL GQTGLP  
 QGPSEQKVAVVTVDGCDTGVALRFGSVLGNYSCAAQGTQGGGSKKSLDLTG PLLGGV  
 PDLPE SFPVRMRQFVGCMRNLQVDSRHIDMADFIANNGTVPGCPAKKNVCDSNTCHN  
 GGTCVNQWDAFSCECPLGFGGKSCAQEMANPQHFLGSSLVAWHGLSLPISQPWYLSL  
 MFRTRQADGVLLQAITRGRSTITLQLREGHVMLSVEGTGLQASSLRLEPGRANDGDWH  
 HAQLALGASGGPGHAILSFDY GQQRAEGNLGPRLHGLHLSNITVGGIPGPAGGVARGF  
 RGCLQGVRVSDTPEGVNSLDP SHGESINVEQGCSLPDPCDSNPCPANSYCSNDWDSY  
 SCSCDPGYYGDNCTNVCDLNPCEHQSVCTRKPSAPHGYTCECPPNYLGPYCETR IDQ  
 PCPRGWWGHPTCGPCNCDVSKGFDPCNKTSGECHCKENHYRPPGSP TCLLCDYCYP  
 TGSLSRVCDPEDGQCPCPKPGVIGRQC DRCDNPFAEVT TNGCEVNYDSCPRAIEAGIW  
 WPRTRFGLPAAAPCPKGSFGTAVRH CDEHRGWLPPNLFNCT SITFSELKGFAERLQRN  
 ESGLD SGRSQQ LALLRNATQHTAGYFGSDVKVAYQLATRLLAHESTQRGFGLSATQD  
 VHFTENLLRVGSALLDTANKRHWELIQQTEGGTAWLLQH YEAYASALAQNMRHTYLSP  
 FTIVTPNIVISVVR LDKGNFAGAKLP RYEALRGEQPPDLETTVILPESVFRET PPVVRPAG  
 PGEAQEPEELARRQRRHPELSQGEAVASVIIYRTL AGLLPHNYDPDKRSLRVPKRPIINT

PVVSISVHDDEELLPRALDKPVTQFRLLTEERTKPICVFWNHSILVSGTGGWSARGC  
 EVVFRNESHVSCQCQCNHMTSFAVLMDVSRRENGEILPLKTLTYVALGVTLAALLLTFFFLT  
 LLRILRSNQHGIRRNLTAAALGLAQLVFLGGINQADLPFACTVIAILLHFLYLCTFSWALLEAL  
 HLYRALTEVRDVNTGPMRFYYMLGWGVPAFITGLAVGLDPEGYGNDPFCWLSIYDTLI  
 WSFAGPVAFVSMVFLYILAAASCAAQRQGFEEKKGPVSGLQPSFAVLLLLSATWLLA  
 LLSVNSDTLLFHLYLFATCNCIQGPFIFLSYVVLSKEVRKALKLACSRKPSPDPALTTKSTL  
 TSSYNCPSPYADGRLYQPYGDSAGSLHSTSRSGKSQPSYIPFLLREESALNPGQGPPG  
 LGDPGSLFLEGQDQQHDPDTSDDSDLSLEDDQSGSYASTHSSDSEEEEEEEEEEEAAAF  
 PGEQGWDSLLGPGAERLPLHSTPKDGGPGPGKAPWPGDFGTTAKESSGNGAPEERL  
 RENGDAISREGSLGPLPGSSAQPHKGILKKKCLPTISEKSSLLRPLEQCTGSSRGSSA  
 SEGSRGGPPPRPPPRQSLQEQLNGVMPIAMSIKAGTVDEDSSGSEFLFFNFLH

SEQID No:31

MLRRPAPALAPAARLLLGLLGGGVWAARVNHKHPWLEPTYHGIVTENDNTVLLDPP  
 LIALDKDAPLRFAESFEVTVTKEGEICGFKIHGQNVPFDAVVVDKSTGEGVIRSKEKLDC  
 ELQKDYSFTIQAYDCGKGPDGTNVKKSHKATVHIQVNDVNEYAPVFKEKSYKATVIEGK  
 QYDSILRVEAVDADCSPQFSQICSYEIITPDVPFTVDKDG YIKNTEKLNYGKEHQYKLTVT  
 AYDCGKKRATEDVLVKISIKPTCTPGWQGWNNRIEYEPGTGALAVFPNIHLETCDEPVA  
 SVQATVELETSHIGKGCDRDTYSEKSLHRLCGAAAGTAELLPSPSGSLNWTMGLPTDN  
 GHDSQVFEFNGTQAVRIPDGVVSVSPKEPFTISVWMRHGPFGRRKKETILCSSDKTDM  
 NRHHYSLYVHGCRLIFLFRQDPSEEKKYRPAEFHWKLNQVCDEEWHHYVLNVEFPSVT  
 LYVDGTSHEPFSVTEDYPLHPSKIETQLVVGACWQEFSGVENDNETEPVTVASAGGDL  
 HMTQFFRGNLAGLTLRSGKLADKKVIDCLYTCKEGLDLQVLEDSGRGVQIQAHPSQLVL  
 TLEGEDLGELDKAMQHISYLNRSRQFPTPGIRRLKITSTIKCFNEATCISVPPVDGYVMVLQ  
 PEEPKISLSGVHHFARAASEFESSEGVFLFPELRIISTITREVEPEGDGAEDPTVQESLVS  
 EEIVHDLDTCEVTVEGEELNHEQESLEVDMARLQQKGIEVSSSELGMTFTGVDTMASY  
 EEVLHLLRYRNWHARSLLDRKFKLICSELNGRYISNEFKVEVNVNVIHTANPMEHANHMAA  
 QPQFVHPEHRSFVDLSGHNLNPHPFVAVVPSTATVVIVVCVSFLVFMILGVFRIRAAHR  
 RTMRDQDTGKENEMDWDDSAITITVNPMETYEDQHSSEEEEEEEEEEEEESEEDGEEDD  
 ITSAESESSEEEEEGEQGD PQNATRQQQLEWDDSTLSY

SEQID No:32

MLPGRLCWVPLLLALGVGSGSGGGGGDSRQRRLLAAKVNKHKHPWIETSYHGVITENNDT  
 VILDPPLVALDKDAPVPFAGEICAFKIHGQELPFEAVVLNKTSGEGRLRAKSPIDCELOKE

YTFIIQAYDCGAGPHETAWKKSHKAVVHIQVKDVNEFAPTFKEPAYKAVVTEGKIYDSIL  
 QVEAIDEDCSPQYSQICNYEIVTTDVPFAIDRNGNIRNTEKLSYDKQHQQYEILVTAYDCG  
 QKPAAQDTLVQVDVKPVCKPGWQDWTKRIEYQPGSGSMPLFPSIHLETCDGAVSSLQI  
 VTELQTNYIGKGCDRETYSEKSLQKLCGASSGIIDLLPSPSAATNWTAGLLVDSSEMIFK  
 FDGRQGAKIPDGIVPKNLTDQFTITMWMKHGPPSPGVRAEKETILCNSDKTEMNRHHYAL  
 YVHNCRLVFLLRKDFDQADTFRPAEFHWKLDQICDKEWHYYVINVEFPVVTLYMDGAT  
 YEPYLVTDNWPIHPSHIAMQLTVGACWQGGGEVTKPQFAQFFHGSASLTIRPGKMESQ  
 KVISCLQACKEGLDINSLESLGQGKIYHFNPSQSILVMEGDDIGNINRALQKVSYSINSRQF  
 PTAGVRRLLKVSSKVQCFCGEDVCISIPEVDAYVMVLQAIEPRITLRGTDHFWRPAAQFES  
 ARGVTLFPDIKIVSTFAKTEAPGDVKTTPKSEVLEEMLHNLD FCDILVIGGDLDPRQECL  
 ELNHSELHQRHLDATNSTAGYSIYGVGSMSTRYEQVLHHIRYRNWRPASLEARRFRIKC  
 SELNGRYTSNEFNLEVSILHEDQVSDKEHVNHLIVQPPFLQSVHHPESSRSIQHSSVVP  
 SIATVVIISVCMLVFVAMGVYRVRIAHQHFIQETEAAKESEMDWDD SALTITVNPMEKH  
 EGPGEHGEDETEGEEEEEEAEEEMSSSSSGSDDEEEEEEEEGMGRGRHGGQNGARQAQL  
 EWDDSTLPY

SEQID No:33

MTLLLLPLLLASLLASCSCNKANKHKPWIEAEYQGIVMENDNTVLLNPPLFALDKDAPLR  
 YAGEICGFRLHGSGVPFEAVILDKATGEGILRAKEPVDCEAQKEHTFTIQAYDCGEGPD  
 GANTKKSHKATVHVRVNDVNEFAPVFVERLYRAAVTEGKLYDRILRVEAIDGDCSPQYS  
 QICYEILTPNTPFLIDNDGNIENTEKLQYSGERLYKFTVTAYDCGKKRAADDAEVEIQVK  
 PTCKPSWQGWNKRIEYAPGAGSLALFPGIRLETCD EPLWNIQATIELQTSHVAKGCDRD  
 NYSERALRKLCGAATGEVDLLPMPGPANWTAGLSVHYSQDSSLIYWFNGTQAVQVP  
 LGGPSGLGSGPQDSLSDHFTLSFWMKHGVTNKGKKEEETIVCNTVQNEDEGFSHYSLT  
 VHGCRIAFLYWPLLESARPVKFLWKLEQVCDD EWHHYALNLEFPTVTLYTDGISFDPALI  
 HDNGLIHPPRRPALMIGACWTEENKEKEKGDNSTDTTQGDPLSIHHYFHGYLAGFS  
 VRSGRLESREVIECLYACREGLDYRDFESLGKGMKVHVNPSQSLLTLEGDDVETFNHA  
 LQHVAYMNTLRFATPGVRPLRLTTAVKCFSEESC VSIPEVEGYVVVLQPDAPQILLSGTA  
 HFARPAVDFEGTNGVPLFPDLQITCSISHQVEAKKDES WQGTVTDTRMSDEIVHNLDG  
 CEISLVGDDLDPERESLLLDTTSLQQRGLELTNTSAYLTIAGVESITVYEEILRQARYRLR  
 HGAALYTRKFRLSCSEMNGRYSSNEFIVEVNV LHSMNRVAHPSHVLSSQQFLHRGHQP  
 PPEMAGHSLASSHRNSMIPSAATLIIVVCVGLVLMVVLGLVRIHSLHRRVSGAGGPPGA  
 SSDPKDPDLFWDD SALTIIIVNPMESYQNRQSCVTGAVGGGQGEDEDSSDSEVADSPSS  
 DERRIETPPHRY



SEQID No:34

MYIKQVIIQGFRSYRDQTIVDPFSSKHNIVGRNGSGKSNFFYAIQFVLSDEFSHLRPEQ  
 RLALLHEGTGPRVISAFVEIIFDNSDNRLPIDKEEVSLRRVIGAKKDQYFLDKKMVTKNDV  
 MNLLESAGFSRSPYYIVKQGKINQMATA PD SQRLKLLREVAGTRVYDERKEESISLMK  
 ETEGKREKINELLKYIEERLHTLEEEKEELA QYQKWDKMRRALEYTIYNQELNETRAKLD  
 ELSAKRETSGEKSRQLRDAQQDARDK MEDIERQVRELKTKISAMKEEKEQLSAERQEQ  
 IKQRTKLELKA KDLQDEL AGNSEQRKRLLKERQKLLEKIEEKQKELAETEPKFNSVKEKE  
 ERGIARLAQATQERTDLYAKQGRGSQFTSKEERDKWIKKELKSLDQAINDKKRQIAAIHK  
 DLEDTEANKEKNLEQYNKLDQDLNEVKARVEELDRKYEEVKNKKDELQSERNYLWREE  
 NAEQQALAAKREDLEKKQQLLRAATGKAILNGIDSINKVLDHFRRKGINQHVGNGYHGIV  
 MNNFECEPAFYTCVEVTAGNRLFYHIVDSDEVSTKILMEFNKMNLPGEVTFPLPLNKLDV  
 RDTAYPETNDAIPMISKLRYNPRFDKAFKHVFGKTLICRSMEVSTQLARAFTMDCITLEG  
 DQVSHRGALTGGYYDTRKSRLELQKDVRKAEEELGELEAKLNENLRRNIERINNEIDQL  
 MNQMQQIETQQRKFKASRDSILSEMKMLKEKRQQSEKTFMPKQRSLSLEASLHAME  
 STRESLKAELGTDLLSQLSLEDQKRVDALNDEIRQLQQENRQLLNERIKLEGIITRVETYL  
 NENLRKRLDQVEQELNELRETEGGTVLTATTSELEAINKRVKDTMARSEDLDNSIDKTE  
 AGIKELQKSMERWKNMEKEHMDAINHDTKELEKMTNRQGMILLKKKEECMKKIRELGSL  
 PQEAFEKYQTL SLKQLFRKLEQCNTTELKKYSHVNKKALDQFVNFSEQKEKLIK RQEELD  
 RGYKSIMELMNVLELRKYEAIQLTFKQVSKNFSEVFQKLVPGGKATLVMKKGDVEGSQS  
 QDEGE GSGESER GSGSQSSVPSVDQFTGVGIRVSFTGKQGEMREMQLSGGQKSLV  
 ALALIFAIQKCDPAPFYLFDEIDQALDAQHRKAVSDMIMELAVHAQFITTTFRPELLESAD  
 KFYGVKFRNKVSHIDVITAEMAKDFVEDDTTHG

SEQID No:35

MAVTLDKDAYYRRVKRLYSNWRKGEDEYANVDAIVSVGVDEEIVYAKSTALQTWLFG  
 YELTDTIMVFCDDKIIFMASKKKVEFLKQIANTKGNENANGAPAITLLIREKNESNKSSFD  
 KMIEAIKESKNGKKIGVFSKDKFPGEFMKSWNDCLNKEGFDKIDISAVVAYTIAVKEDGE  
 LNLMKKAASITSEVFNKFFKERVMEIVDADEKVRHSLAESVEKAIEEKKYLAGADPSTV  
 EMCYPPIIQSGGNYNLKFSSVSDKNHMHFGAITCAMGIRFKSYCSNLVRTLMVDPSQEV  
 QENYNFLLQLQEELLKELRHGVKICDVYNAVMDVVKKQKPELLNKITKNLGFGMGIEFR  
 EGSLVINSKNQYKLKKG MVFSINLGFSDLTNKEGKKPEEKTYALFIGDTVLVDEDGPATV  
 LTSVKKKVKNVGIFLKNEDEEEEEEEEKDEAEDLLGRGSRAALLTERTRNEMTAEEKRRA  
 HQKELAAQLNEEAKRRLTEQKGEEQQIQKARKSNVSYKNPSLMPKEPHIR



EMKIYIDKKYETVIMPVFGIATPFHIATIKNISM SVEGDYTYLRINFYCPGSALGRNEGNIF  
 PNPEATFVKEITYRASNIKAPGEQTVPALNLQNAFRIIKEVQKRYKTREAEKEKEGIVKQ  
 DSLVINLNRSNPKLKDLYIRPNIAQKRMQGSLEAHVNGFRFTSVRGDKVDILYNNIKHAL  
 FQPCDGEMIIVLHFHLKNAIMFGKKRHTDVQFYTEVGEITDLGKHQHMHDRDDLYAEQ  
 MEREMRHLKLTAFKNFIEKVEALTKEELEFEVPFRDLGFNGAPYRSTCLLQPTSSALVN  
 ATEWPPFVVTLDLEVELHFERVQFHLKNFDMVIVYKDYSKKVTMINAIPVASLDPIKEWLN  
 SCDLKYTEGVQSLNWTIMKTIVDDPEGFFEQQGGWSFLEPEGEGSDAEEGDSESEIED  
 ETFNPSEDDYEEEEEDSDEDYSSEAEESDYSKESLGSEEEESGKDWDELEEEEARADR  
 ESRYYYYEEQSRSMSRKRKASVHSSGRGSRNRGSRHSSAPPKKKRK

SEQID No:36

MVVSKMNKDAQMRAAINQKLIETGERERLKELLRAKLIECGWKDQLKAHCKEVIKEKGL  
 EHVTVDLVAEITPKGRALVPDSVKKELLQRIRTFLAQHASL

SEQID No:37

MENHKSNNKENITIVDISRKINQLPEAERNLLENGSVYVGLNAALCGLIANS LFRRILNVT  
 KARIAAGLPMAGIPFLTTLTYRCFVSFPLNTGDLDCETCTITRSGLTGLVIGGLYPVFLAI  
 PVNGGLAARYQSALLPHKGNILSYWIRTSKPVFRKMLFPILLQTMFSAYLGSEQYKLLIK  
 ALQLSEPGKEIH

SEQID No:38

MAEVEETLKRLQSQKGVQGIIVNTEGIPIKSTMDNPTTTQYASLMHSFILKARSTVRDID  
 PQNDLTFLRIRSKKNEIMVAPDKDYFLIVIQNPTE

SEQID No:39

MAAVGRVGSFGSSPPGLSSTYTGGPLGNEIASGNGGAAAGDDEDGQNLWSCILSEVS  
 TRSRSKLPAGKNVLLLGEDGAGKTSIRKIQQIEEYKKGRGLELYLNVHDEDRDDQTR  
 CNVWILDGDLYHKGLLKFSLDVSLKDTLVMLVVDMSKPWTALDSLQKWASVVREHVD  
 KLIKIPPEEMKQMEQKLIRDFQEYVEPGEDFPASPQRRNTASQEDKDDSVVVPLGADTL  
 THNLGIPVLVVCTKCDASVLEKEHDYRDEHFDFFQSHIRKFCLRYGAALIYTSVKENKNI  
 DLVYKYIVQKLYGFPYKIPAVVVEKDAVFIPAGWDNDKKIGILHENFQTLKAEDNFEDIITK  
 PPVRKFVHEKEIMAEDDQVFLMKLQSLAKQPPTAAGRPVDASPRVPGGSPRTPNRSV  
 SSNVASVSPIPAGSKKIDPNMKAGATSEGVLANFFNSLLSKKTGSPGGPGVSGGSPAG  
 GAGGGSSGLPPSTKKSGQKPVLDVHAELDRITRKPVTVSPTTPTSPTEGEAS

SEQID No:40

MVTQILGAMESQVGGGPAGPALPNGPLLGTNGATDDSKTNLIVNYLPQNMTQDEFKSL  
 FGSIGDIESCKLVRDKITGQSLGYGFVNYS DPNDADK AINTLNGLKLQTKTIKVS YARPSS  
 ASIRDANLYVSGLPKTMSQKEMEQLFSQYGRITSRILVDQVTGVSRGVGFIRFDKRIEA  
 EEAIKGLNGQKPLGAAEPITVKFANNPSQKTGQALLTHLYQSSARRYAGPLHHQTQRFR  
 LDNLLNMAYGVKSPLSLIARFSPIAIDGMSGLAGVGLSGGAAGAGWCIFVYNLSPEADE  
 SVLWQLFGPFGAVTNVKVIRDFTTNKCKGFGFVTMTNYDEAAMAIASLNGYRLGERVL  
 QVSFKTSKQHKA

SEQID No:41

MVCTCVEGDNQFIVTEIPHVRQLISGDGVGEC AVRAATEGRTLILEGLEKAERNVLPVLN  
 NLENREMQLEDGRFLMSAERYDKLLRDHTKKELDSWKIVRVSENFRVIALGLPVP RYS  
 GNPLDPPLRSRFQARDIYYLPFKDQLKLLYSIGANVSAEKVSQLLSFATT LCSQESSTLG  
 LPDFPLDSLAAAVQILDSFPMMPIKHAIQWLYPYSILLGHEGKMAVEGV LKRFELQDSGS  
 SLLPKEIVKVEKMMENHVSQASVTIRIADKEVTIK

SEQID No:42

MSASQDSRSRDNGPDGMEPEGVIESNWN EIVDSFDDMNLSESLLRGIYAYGF EKPSAI  
 QQRAILPCIKGYDVIAQAQSGTGKTATFAISILQQIELDLKATQALVLAPTRELAQQIQKV  
 MALGDYMGASCHACIGGTNVRAEVQKLQMEAPHIIVGTPGRVFDMLNRRYLSPKYIKM  
 FVLDEADEMLSRGFKDQIYDIFQKLNSNTQVVLLSATMPSDVLEVTKKFMRDPIRILVKK  
 EELTLEGIRQFYINVEREEWKLDLTLCDLYETLTITQAVIFINTRRKVDWLTEKM HARDFTV  
 SAMHGDMQKERVIMREFRSGSSRVLITTDLLARGIDVQQVSLVINYDLPTNRENYIH  
 RIGRGGRFGRKGVAINMVTEEDKRTL RDIETFYNTSIEEMPLNVADLI

SEQID No:43

MDQCVTVERELEKVLHKFSGYGQLCERGLEELIDYTGGLKHEILQSHGQDAELSGT LSL  
 VLTQCCKRIKDTVQKLASDHKDIHSSVSRVGKAIDKNFDS DISSVGIDGCWQADSQRLL  
 NEVMVEHFFRQGMLDVAEELCQESGLSVDPSQKEPFVELNRILEALKVRVLRPALEWA  
 VSNREMLIAQNSSLEFKLHRLYFISLLMGGTTNQREALQYAKNFQPFALNHQKDIQVLM  
 GSLVYLRQGIENSPYVHLLDANQWADICDIFTRDACALLGLSVESPLSVSFSAGCVALPA  
 LINIKAVIEQRQCTGVWNQKDELPIEVDLGKKCWYHSIFACPILRQQTTDNNPPMKLVCG  
 HIISRDALNKM FN GSKLKCPYCPMEQSPGDAKQIFF

SEQID No:44

MLGTGPAAATTAATTSSNVSVLQQFASGLKSRNEETRAKAAKELQHYVTMELREMSQE  
ESTRFYDQLNHHIFELVSSSDANERKGGILAIASLIGVEGGNATRIGRFANYLRNLLPSND  
PVVMEMASKAIGRLAMAGDTFTAHEYVEFEVKRALEWLGAADRNEGRRHAAVLVLRELAI  
SVPTFFFQQVQPFFDNIFVAVWDPKQAIREGAVAALRACLILTTQREPKEMQKPQWYR  
HTFEEAEKGFDETLAKEKGMNRDDRIHGALLILNELVRISSEMEGERLREEMEEITQQQLV  
HDKYCKDLMGFGTKPRHITPFTSFQAVQPQQSNALVGLLGYSSHQGLMGFGTSPSPAK  
STLVESRCCRDLMEEKFDQVCQWVLKCRNSKNSLIQMTILNLLPRLAAFRPSAFTDTQY  
LQDTMNHVLSVCVKKERKERTAAFQALGLLSVAVRSEFKVYLPRVLDIIRAALPPKDFAHKR  
QKAMQVDATVFTCISMLARAMGPGIQQDIKELLEPM LAVGLSPALTAVLYDLSRQIPQLK  
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VLVRHRINHQRVDVLCRIVKGYTLADEEEDPLIYQHRMLRSGQG DALASGPVETGPMK  
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RDLFNAAFVSCWSELNEDQQDELIRSIELALTSQDIAEVTQTLLNLAEFMEHSDKGPLPL  
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GNNLQDTRLRVLTWFDYGHWPDVNEALVEGVKAIQIDTWLQVIPQLIARIDTPRPLVGRL  
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 EKFPKIPFRLTRMLTNAMEVTGLDGNYRITCHTVMEVLREHKDSVMAVLEAFVYDPLL  
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 CFW

SEQID No:45

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 VAVVIVDPQGRRDTVEVALEDKGDSTFRCTYRPAMEGPHTVHVAFAGAPITRSPFPVH  
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 VREAGDGVFECEYYPVPGKYVVTITWGGYAIPRSPFEVQVSPEAGVQKVRAWGPGL  
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GEAATFTVDCSEAGEAELTIELSDAGVKAEVLIHNNADGTYHITYSPAFFPGTYTITIKYGG  
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 VNTLNAGSGALSVTIDGPSKVQLDCRECPEGHVVTYTPMAPGNYLIAIKYGGPQHIVGS  
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SEQID No:46

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 PENSRLRVLLGAPNAGKSTLSNQLLGRKVFPVSRKVHTTRCQALGVITEKETQVILLD  
 TPGIISPGKQKRHHLELSLLEDPWKSMESADLVVVLVDVSDKWTRNQLSPQLLRCLTKY  
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DPNTQSVGNPQRIGWPHFKEIFMLSALSQEDVKTLLKQYLLTQAQPGPWEYHSAVLT SQ  
TPEEICANIIREKLLLEHLPQEV PYNVQQKTAVWEEGPGGELVIQQKLLVPKESYVKLLIGP  
KGHVISQIAQEAGHDLMDIFLCDVDIRLSVKLLK

SEQID No:47

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LDVNLMGTFNVIRLVAGEMGQNEPDQGGQRGVIINTASVAAFEGQVGQAAYSASKGGI  
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SEQID No:48

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DESYGQIFKPIISKVMEMYQPSAVVLQCGADSLSGDRLGCFNLTVKGHAKCVEVVKTFN  
LPLLMLGGGGYTIRNVARCWYETAVALDCEIPNELPYNDYFEYFGPDFKLHISPSNMT  
NQNTPEYMEKIKQRLFENLRMLPHAPGVQMMAIPEDAVHEDSGDEDEDGEDPDKRISIRA  
SDKRIACDEEFSDSEDEGEGERRNVA DHKKGAKKARIEEDKKETEDKKTDVKEEDKSK  
DNSGEKTDTKGTKSEQLSNP

SEQID No:49

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SVLVKEQQALAVQSATTTLSALRLKQRLVILERYFIALNRTVFQENVKVWKSSGISLPP  
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LPEASLFDESTVSSVWLEVVERATRFLRSVVTGDVHGTPATKGPGSIPLQDQHLALAILL  
ELAVQRGTL SQMLSAILLLLQLWDSGAQETDNERSAQGTSAPLLPLLQRFQSIICRKDAP  
HSEGDMHLLSGPLSPNESFLRYLTLPQDNELAI DL RQTAVVVM AHLDRLATPCMPPLCS  
SPTSHKGS LQEVIWGLIGWKYYANVIGPIQCEGLANLGVTQIACA EKRFLILSRNGRVY  
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APVECP SFSSAAPSDASAMASPMNGEECMLAVDIEDRLSPNPWQEKREIVSSEDAVTP  
SAVTPSAPSASARPFIPVTDDLGAASIIAETMTKTKEDVESQNKAAGPEPQALDEFTSLLI  
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LPRLFLDEVAKKIRELMADSENMDVLHESHDIKREQDEQLVQWMNRRPDDWTLSAG  
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RRPRQVQGLQGKKVIAIATGSLHCVCCTEDGEVYTWGDNDEGQLGDGTTNAIQRPRLV  
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ATSEEF EAMSLPFTVPSASGQDIQLSSKH THITLDNRAEYVRLAINYRLHEFDEQVA AVR



EGMARVVPVPLLSLFTGYELETMVCGSPDIPLHLLKSVATYKGIEPSASLIQWFWEVME  
 SFSNTERSLFLRFVWGRTRLPRTIADFRGRDFVIQVLDKYNPPDHFLPESYTCFFLLKLP  
 RYSCKQVLEEKLYAIHFCKSIDTDDYARIALTGEPAAADDSSDDSDNEDVDSFASDSTQ  
 DYLTGH

SEQID No:50

MICTFLRAVQYTEKLHRSSAKRLLLPYIVLNKACKTEPSLRGGLQYQKKTLRPRCILGVT  
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 TGGLFYTIFKELFSSSSPSKIYGRALEKCRSHPEVIGVFGESVKGYGEVTRRGRRQHV  
 FTEYVKDGLKHTCVKFYIEGSEPGKQGTVYAQVKENPGSGEYDFRYIFVEIESYPRRTII  
 EDNRSQDD

SEQID No:51

MAATSGTDEPVSGELVSVAHALSIPAESYGNDPDIEMAWAMRAMQHAEVYYKLISVD  
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 TLLRLDCSQGYTEENTIFAPRIQFFAIEIARNREGYNKAVYISVQDKEGEKGVNNGGEKR  
 ADSGEEENTKNGGEKGADSGEEKEEGINREDKTDKGGEKGKEADKEINKSGEKAM

SEQID No:52

MSQRDTLVHLFAGGCGGTVGAILTCPLEVVKTRLQSSSVTLYISEVQLNTMAGASVNRV  
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 QVHMISAAMAGFTAITATNPIWLIKTRLQLDARNRGERRMGAFECVRKVYQTDGLKGFY  
 RGMSASYAGISETVIHFVIYESIKQKLLEYKTASTMENGEESVKEASDFVGMMLAAATSK  
 TCATTIAYPHVVRTRLREEGTKYRSFFQTLSELLVQEEGYGSLYRGLTTHLVRQIPNTAIM  
 MATYELVVYLLNG

SEQID No:53

MSQFKRQRINPLPGGRNFSGTASTSLLGPPPGLLTPPVATELSQNARHLQGGEKQRVF  
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 HLNRFPARGPHGRLDQGRSDDYDSKKRKQRAGGEPWGAKKPRHDLPPYRVHLTPYT  
 VDSPICDFLELQRRYRSLLVPSDFLSVHLSWLSAFPLSQPFSLHHPSRIQVSSEKEAAPD  
 AGAEPITADSDPAYSSKVLLLSSPGLEELYRCCMLFVDDMAEPRETPEHPLKQIKFLLGR  
 KEEEAVLVGGEWSPSLDGLDPQADPQVLVRTAIRCAQAQTGIDLSGCTKWWRFAEFQ

YLQPGPPRRLQTVVVYLPDVWTIMPTLEEWEALCQQKAAEAAPPTQEAQGETEPTQA  
 PDALEQAADTSRRNAETPEATTQQETDSDLPEAPPPPLEPAVIARPGCVNLSLHGIVED  
 RRPKERISFEAGVMVLAELFLEMLQRDFGYRVYKMLLSLPEKVVSPPEPEKEEAAKEEA  
 TKEEEAIKEEVVKEPKDEAQNEGPATESEAPLKEDGLLPKPLSSGGEEEEKPRGEASED  
 LCEMALDPELLLLRDDGEEEFAGAKLEDSEVRSVASNQSEMEFSSLQDMPKELDPSAV  
 LPLDCLLAFVFFDANWCGYLHRRDLERILLTLGIRLSAEQAKQLVSRVVTQNICQYRSLQ  
 YSRQEGLDGGLPEEVLFGNLDLLPPPGKSTKPGAAPTEHKALVSHNGSLINVGSLQRA  
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SEQID No:54

MAPIGLKAVVGEKIMHDDVIKKVKKKGWVKLVVDQLSMRMLSSCCKMTDIMTEGITIVED  
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 KEYPAVRYRGEYKDNALLAQLIQDKLDAYKADDPTMGEGPDKARSQLLILDRGFDPSSP  
 VLHELTFQAMSYDLLPIENDVYKYETSGIGEARVKEVLLDEDDDLWIALRHKHIAEVSQE  
 VTRSLKDFSSSKRMNTGEKTTMRDLSQMLKKMPQYQKELSKYSTHLHLAEDCMKHYYQ  
 GTVDKLCRVEQDLAMGTDAEGEKIKDPMRAIVPILLDANVSTYDKIRIILLYIFLKNGITEE  
 NLNKLIQHAQIPPEDSEITNMAHLGVPIVTDSTLRRRSKPERKERISEQTYQLSRWTPPIK  
 DIMEDTIEDKLDTKHYPYISTRSSASFSTTAVSARYGHHKNKAPGEYRSGPRLIIFILGG  
 VSLNEMRCAYEVTQANGKWEVLIGSTHILTPTKFLMDLRHPDFRESSRVSFEDQAPTM  
 E

SEQID No:55

VAGVRPSSPHGLVGAVSVGGAGVMAVETLSPDWEFDRVDDGSQKIHAEVQLKNYGKF  
 LEEYTSQLRRIEDALDDSIGDVWDFNLDPIALKLLPYEQSSLLELIKTENKVLNKVITVYAA  
 LCCEIKKLKYEATKFYNGLLFYGEGATDASMVEGDCQIQMGRFISFLQELSCFVTRCY  
 EVVMNVVHQLAALYISNKIAPKIIETTGVHFQTMYEHLGELLTVLLTLDEIIDNHITLKDHW  
 TMYKRLLKSVHHNPSKFGIQEEKLKPFEKFLKLEGQLLDGMIFQACIEQQFDSLNGGVS  
 VSKNSTFAEEFAHSIRSIFANVEAKLGEPSEIDQRDKYVGICGLFVLHFQIFRTIDKKFYKS  
 LLDICKKVPAILTANIIWFPDNFLIQKIPAAAKLLDRKSLQAIAKIHRDTFLQQKAQSLTKDV  
 QSYYVVFVSSWMMKMESILSKEQRMDKFAEDLTNRCNVFIQGFYAYSISTIIKTMTNLYM  
 SMQKPMTKTSVKALCRLVELLKAIEHMFYRRSMVVADSVSHITQHLQHQAALHSISVAKK  
 RVISDKKYSEQRLDVLSALVLAENTLNGPSTKQRRRLIVSLALSVGTQMKTFFKDEELFPLQ

VVMKKLDLISELRERVQTQCDCCFLYWHRAVFPIYLDDVYENAVDAARLHYMFSA LRDC  
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 VGMKDLALFFSLNPIRFFNRFIDIRAYVTHYLDKTFYNLTVALHDWATYSEMRNLATQR  
 YGLVMTEAHLPSQTLEQGLDVLEIMRNIHIFVSRYLYNLNNQIFIERTSNNKHLNTINIRHI  
 ANSIRTHGTGIMNTTVNFTYQFLKKKFYIFSQFMYDEHIKSRLIKDIRFFREIKDQNDHKY  
 PFDRAEKFNRGIRKLGITPEGQSYLDQFRQLISQIGNAMGYVRMIRSGGLHCSSNAIRFV  
 PDLEDIVNFEELVKEEGLAEETLKAARHLDSVLSDHTRNSAEGTEYFKMLVDVFAPEFR  
 RPKNIHLRNFYIIVPPLTLNFVEHSISCKEKLNKKNKIGAAFTDDGFAMGVAYILKLLDQYR  
 EFDSLHWFQSVREKYLKEIRAVAKQQNVQSASQDEKLLQTMNLTQKRLDVYLQEFELL  
 YFSLSSARIFFRADKTAAEENQEKKKEEETKTSNGDLS DSTVSADPVVK

SEQID No:56

MRLKLFSILSTALLRATDTINSQGQFPSYLETVTKDILAPNLQWHAGR TAAAIRTA AVSCL  
 WALTSSSEVL SAEQIRDVQETLMPQVLT TLEEDSKMTRLISCR IINTFLKTSGGMTDPEKLI  
 KIYPELLKRLDDVSNDVRMAAASTLV TWLQCVKGANAKSYYQSSVQYLYRELLVHLDDP  
 ERAIQDAILEVLKEGSGLFPDLLVRETEAVIHKHRSATYCEQLLQH VQAVPATQ

SEQID No:57

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 SPDQELVLLATGQQTLIMMTKDFEPILEQQIHQDDFGESKFITVGWGRKETQFHGSEGR  
 QAAFQM QMHESALPWDDHRPQVTWRGDGQFFAVSVVCPETGARKVRVWNREFALQ  
 STSEPVAGLGPALAWKPSGSLIASTQDKPNQQDIVFFEKNGLLHG HFTLPFLKDEVKVN  
 DLLWNADSSVLAVRLEDLQREKSSIPKTCVQLWTVGN YHWYLKQSLSFSTCGKSKIVSL  
 MWDPVTPYRLHVLCQGWHYLA YDWHWTDRSVGDNSSDLSNV AVIDGNRVLVTVFR  
 QTVVPPPMCTYQLLFPHPVNQVTFLAHPQKSNDLAVLDASNQISVYKCGDCPSADPTV  
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 SPRSVIHHLTAASSEMDEEHGQLNVSSSAAVDGVII SLCCNSKTKSVVLQLADGQIFKYL  
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 SFAVYDEFLLLTTHSHTCQCFC LRDASFCTLQAGLSSNHVSHGEVLRKVERGSRIVTVV  
 PQDTKLVLQMPRGNLEV VHHRALVLAQIRKWLDKLMFKEAFECMRKLRINLNPIYDHNP  
 KVFLGNVETFIKQIDSVNHINLFFTELKEEDVT KTMYPAPVTSSVYLSRDPDGNKIDLVCD  
 AMRAVMESINPHKYCLSILTSHVKKTTPELEIVLQKVHELQGNAPSDPD AVSAEEALKYL  
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KRYEKAIGHLSKCGPEYFPECLNLIKDKNLYNEALKLYSPSSQQYQDISIAYGEHLMQEH  
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 KNYMAFLDSQTATFSRHKKRLLVVRELKEQAQQAGLDDEVPHGQESDLFSETSSVVS  
 SEMSGKYSHSNSRISARSSKNRRKAERKKHSLKEGSPLEDLALLEALSEVVQNTENLKD  
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SEQID No:58

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 GKEGTHATCASEEGGTESESSESGSSLQPFSAADSTPDVNQSPRGKRRAKAGSRSRNSTL  
 TSLCVLSHYPFFSTFRECLYTLKRLVDCCSERLLGKKLGIPRGVQRDTMWRIFTGSLLE  
 EKSSALLHDLREIEAWIYRLLRSPVPVSGQKRVDIEVLPQELQPALTFALPDPSRFTLVDF  
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 PTCMASAEQLLLAPTPYIIGVPASFFLYKLDFKMPDDVWLVDLDSNRVIAPTNAEVLPILP  
 EPESLELKKHLKQALASMSLNTQPILNLEKFHEGQEIPLLLGRPSNDLQSTPSTEFNPLIY  
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 PSTVIHGANSEPADSTEMDDKAAVGVSKPLPSVPPSIGKSNVDRRQAEIGEGSVRRRIY  
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 SRASSPNSTVSNTSTEGFGGIMSFASSLYRNHSTSFSLSNLTLP TKGAREKATPFPSLK  
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 VEISRKVYKGMLDLLKCTVLSLEQSYAHAGLGGMASIFGLLEIAQTHYYSKEPDKRKRSP  
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 YLSLGEHDRKRLEDDERLLATLLHNLISYMLLMKVNKNDIRKKVRRRLMGKSHIGLVYSQ  
 QINEVLDQLANLNGRDLSIWSSGSRHMKKQTFVVHAGTDTNGDIFFMEVCDDCVLRS



NIGTVYERWWYEKLINMTYCPKTKVLCLWRRNGSETQLNKFYTKKCRELYYCVKDSME  
 RAAARQQSIKPGPELGGEFPVQDLKTGEGGLLQVTLEGINLKFMHNQVFIELNHIKKCNT  
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SEQID No:59

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 YGLHAAGLYFLLLEVPGSVANQVFHPVMFDKCIQTLKKSWPQESNLNRKRKKEQPKSS  
 QANPGRHRKRGRKPPRRREDIEMDEIIEEQEDENICFSARDLSQIRNAIFHLLKNFLRLLPKF  
 SLKEKPQCVQNCIEVFVSLTNFEPVLHECHVTQARALNQAKYIPELAYYGLYLLCSPHIG  
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 PVVRILLQHICAKVVDKSEYRTFAAQSLVQLLSKLPCGEYAMFIAWLYKYSRSSKIPHRV  
 FTLDVVLALLELPEREVDNTLSLEHQKFLKHKFLVQEIMFDRCLDKAPTVRSKALSSFAH  
 CLELTVTSASESILELLINSPTFSVIESHPGTLLRNSSAFSYQRQTSNRSEPSGEINIDSSG  
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 LEVCEDVAVRNNVIIVMCDLCIRYTIMVDKYIPNISMCLKDSDPFIRKQTLILLTNLLQEEFV  
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 NKFPQSEREKRLFSLKGKSNKERRMKIYKFLLEHFTDEQRFNITSKICLSILACFADGILPL  
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 MKKYQEQLVQEQLAKHADVAGTAGGAEVAPVAQVALCLETVPVPAGQENPAMSPAV  
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 SLGVLPFTLNSGSPEKTCSQVSSYSLEQESNGEIEHVTKRAISTPEKSISDVTFGAGVSYI  
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 KTPLKTAN

SEQID No:60

MWNDIELLTNDDTGSGYLSVGSRKEHGTYLYQVDLLVKISSEKASLNPKIQACSLSDGFI

IVADQSVILLDSICRSLQLHLVFDTEVDVVGLCQEGKFLLVGERSGNLHLIHVTSKQTLLT  
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STAKKLQGQIKSSFISTENYHTLGCLSLVAGDLASEVPVIIGGTGNCAFSKWEPDSSKKG  
MTVKNLIDAEIIGKAKKFQLIDNLLFVLDTDNVLSLWDIYTLTPVWNWPSLHVEEFLLTTE  
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RMFDKVLAPELIPSILEKFIRVYMREHDLQEEELLLYIEDLLNRCSSKSTSLFETAWEAK  
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HEVAQAKHKPGSTPEPIAAEVRSPSMESKLHRQALALQMSKQELEAELTLRALKDGNIK  
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LQESSQWELALRFVVGSGTCLQHSVSNFMNATLSEKLFGETTLVKSRHVVMELKEKA  
VIFIRENATTLLHKVFNCRLVDLDLALGYCTLLPQKDVFENLWKLIDKAWQNYDKILASLV  
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KVWDMLEKWLC PSTKPGEKPSELFELQEDEALRRVQYLLLSRPIDYSSRMLFVFATST  
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ELFCSSPKEGMIKGLWKNHSHESMAVRLVTELCLEYKIYDLQLWNGLLQKLLGFNMIPY  
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QLAGFSHQIRSLILNNIINKKEFGILAKTKYFQMLKMHAMNTNNITELVNYLANDLSLDEA  
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SEQID No:61

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 EYLSNADERLRWQASSLPADDLCTENAIMLKRFNRYPLIIDPSGQATEFIMNEYKDRKIT  
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MQEVETVSQQYLPLSTACSSYFTMESLKQIHFLYQYSLQFFLDIYHNVLYENPNLKGVT  
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 FTVDFEIA TKEDPRS FYERGVAVLCTE

SEQID No:62

MQSRLLLLGAPGGHGGPASRRMRLLLRQVVQRRPGGDRQRPEVRLLHAGSGADTGD  
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 RSIAMQYLELTKREVEYIALSRDTTETDLKQRREIRAGTAFYIDQCAVRAATEGRTLILEG  
 LEKAERNVLPVLNNLLENREMQLDGRFLMSAERYDKLLRDHTKKELDSWKIVRVSENF  
 RVIALGLPVPRYSGNPLDPPLRSRFQARDIYYLPFKDQLKLLYSIGANVSAEKVSQLLSF  
 ATTLCSEQESSTLGLPDFPLDSLAAAVQILDSFPMMPKHAIQWLYPYSILLGHEGKMAVE  
 GVLKRFELQDSGSSLLPKEIVKVEKMMENHVSQASVTIRIADKEVTIKVPAGTRLLSQPC  
 ASDRFIQTLSHKQLQAEMMQSHMVKDICLIGGKGCGKTVIAKNFADTLGYNIEPIMLYQD  
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 LSLYDGSRLLREDRYMRLKEELQLSDEQLQKRSIFPIHPSFRIIALAEPVIGSTAHQWL  
 PEFLTMFFFHYMKPLVKSEEIQVIKEKVPNPVQEALDKLLSFTHKLRETQDPTAQSLAAS  
 LSTRQLLRISRRLSQYPNENLHSAVTKACLSRFLPSLARSALAEKNLADATIEINTDDNLEP  
 ELKDYKCEVTSGTLRIGAVSAPIYNAHEKMKVPDVLFYDNIQHVIVMEDMLKDFLLGEHL  
 LLVGNQGVGKNKIVDRFLHLLNRPREYIQLHRDTTVQTLTLQPSVKDGLIVYEDSPLVKA  
 VKLGHILVVDEADKAPTNTVCILKTLVENGEMILADGRRIVANSANVNGRENVVVIHPDF  
 RMIVLANRPGFPFLGNDFFGTGLGDIFSCHAVDNPKPHSELEMLRQYGPVPEPILQKLV  
 AAFGELRSLADQGIINYPYSTREVVNIVKHLQKFPTGLSSVVRNVFDFDSYNNDMREILI

NTLHKYGIPIGAKPTSVQLAKELTLPEQTFMGYWTIGQARSGMQKLLCPVETHHIDIKGP  
 ALINIQEYPIERHEERSLNFTEECASWRIPLDEINIICDIATSHENEQNTLYVVTCNPASLYF  
 MNMTGKSGFFVDFFDIFPRTANGVWHPFVTVAPLGSPKLGQVVLHEQQSNVILLDDTTG  
 RALHRLILPSEKFTSKKPFWWNKEEAETYKMCKEFSHKNWL VFYKEKGNSTVLDVLE  
 GRTHITISLPINLKT VFLVAEDKWLLVESKTNQKYLLTKPAHIESEGSGVCQLYVLKEEPPS  
 TGFGVTQETEF SIPHERKISSDQLSSEHLSSAVEQKIASPNRILSDEKNYATIVVGFPDLMSP  
 SEVYSWKRPSSLHKRSGTDT SFYRGKKKRGTPKQSNCVTLTLD TNQVVRILPPGEVPLK  
 DIYPKDVTPPQTSGYIEVTDLQSKKLRYPPIRSESLSPYTTWLSTISD TDALLAEWDKSG  
 VVTVDMGGHIRLWETGLERLQRSLMEWRNMIGQDDDRNMQITINRD SGEDVSSPKHGK  
 EDPDNMPHVGGNTWAGGTGGRDTAGLGKGKGGPYRLDAGHTVYQVSQA EKDAVPEE  
 VKRAAREMGQRAFQQRLKEIQMSEYDAATYERFSGAVRRQVHSLRIILDNLQAKGKER  
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 RFNRMDGRLERTMEAVCMVMEAFENYEEKFYDIVGHSGDGYNIGLVPMNKIPKDNK  
 QRLEILKTMHAHSQFCMSGDHTLEGTEHAIKEIVKEEADEYFVIVLSDANLSRYGIHPAKF  
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SEQID No:63

MLERKYGGRLVTRHAARTIQTA FRQYQMKNKFERLRSSMSSENRMSSRRIVLSNM RMQF  
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 LEDAFSRQVKSLAESIDDALNCRSLHTEEAPALDAARARDTEPQTALHGMDHRKLDDEM  
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 DTSCRSTPSLERQEQRRLRVEHLPLLTIEPSPDSSVDLSDRSERGSLKRQSAYERSLGG  
 QQGSPKHGPHSGAPKSLPREPELRPRPPRPLDSHLAINGSANRQSKSESDYSDGDN  
 DSINSTSNSNDTINCSSSESSSRDSLREQTLSKQTYHKEARNSWDSPA FSNDEVIRKRHYR  
 IGLNLFNKKPEKGVQYLIERG FVPDTPVGVAHFLLQRKGLSRQMIGEF LGNRQKQFN RD  
 VLDCVVDEMDFSTMELDEALRK FQAHIRVQGEAQKVERLIEAFSQR YCICNPGVVRQFR  
 NPDTIFILAFAILLNTDMYSPNVKPERKMKLEDFIKNLRGVDDGEDIPREMLMGIYERIRK  
 RELKTNEDHVSQVQKVEKLIVGKKPIGSLHPGLGCVLSLPHRRLLVCYCRLFEVPDPNKP  
 QKLGLHQREIFL FNDLLVVTKIFQKKKNSVTYSFRQSFSLYGMQVLLFENQYYPNGIRLT  
 SSVPGADIKVLINFNAPNPQDRKKFTDDLRESIAEVQEME KHRIESELEKQKGVVRPSM  
 SQCSSLKKESGNGTLSRACLDDSYASGEGLKRSALSSSLRDLSEAGKRGRRSSAGSLE  
 SNVEFQPFEPLOPSVLCS

SEQID No:64

MPLKHVLLLLVGCQAWGAGLAYHGCPSCTCSRASQVECTGARIVAVPTPLPWNAMS  
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 QGLDSLESLLLSSNQLLQIQPAHFSQCSNLKELQLHGNHLEYIPDGAFDHLVGLTKNLG  
 KNSLTHISPRVFQHLGNLQVLRLYENRLTDIPMGTFDGLVNLQELALQQNQIGLLSPGLF  
 HNNHNLQRLYLSNNHISQLPPSIFMQLPQLNRLTLFGNSLKELSLGIFGMPNLRELWLY  
 DNHISLDPDNVFSNLRQLQVLILSRNQISFISPGAFNGLTELRELSLHTNALQDLDGNVFR  
 MLANLQNISLQNNRLRQLPGNIFANVNGLMALQLQNNQLENLPLGIFDHLGKLCERLYD  
 NPWRCDSDILPLRNWLLLNPRLGTDTPVPCFSPANVRGQSLIINVNAVPSVHVPEVP  
 SYPETPWYPDTPSYPDTSVSSTTELTSPVEDYTDLTITQVTDDRSVWGMTHAHSGLA  
 AAIVIGIVALACSLAACVGCCKKRSQAVLMQMKAPNEC

SEQID No:65

MRGSHRAAPALRPRGRLWPVLAVLAAAAAAGCAQAAMDECTDEGGRPQRCMPEFVN  
 AAFNVTVVATNTCGTPPEEYCVQTGVTGVTKSCHLCDAGQPHLQHGAFLTDYNNQA  
 DTTWWQSQTMLAGVQYPSSINLTLLHLGKAFDITYVRLKFHTSRPESFAIYKRTREDGPW  
 IPYQYYSGSCENTYSKANRGFIRTGGDEQQALCTDEFSDFSPLTGGNVAFASTLEGRPS  
 AYNFDNSPVLQEWVTATDIRVTLNRLNTFGDEVFNDPKVLKSYYYAISDFAVGGGRCKCN  
 GHASECMKNEFDKLVCNCKHNTYGVDCCKLPFFNDRPWRRATAESASECLPCDCNG  
 RSQECYFDPELYRSTGHGGHCTNCQDNTDGAHCERCENFFRLGNNEACSSCHCSP  
 VGSLSLTCDSYGRCSCKPGVMGDKCDRCQPGFHSLTEAGCRPCSCDPSGSDIECNV  
 ETGRCVCKDNVEGFNCERCKPGFFNLESSNPRGCTPCFCFGHSSVCTNAVGYSVYSIS  
 STFQIDEDGWRAEQRDGSEASLEWSSERQDIAVISDSYFPRYFIAPAKFLGKQVLSYGQ  
 NLSFSFRVDRRDTLSAEDLVLEGAGLRVSVPLIAQGNSYPSETTVKYVFRLHEATDYP  
 WRPALTPFEFQKLLNNLTSIKIRGTYSERSAGYLDDVTLASARPGPGVPATWVESCTCP  
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 CDDGYFGDPLGRNGPVRLCRLCQCSDNIDPNAVGNLNLRLTGECLKCIYNTAGFYCDR  
 CKDGFNPLAPNPADKCKACNCNPYGTMKQQSSCNPVTGQCECLPHVTGQDCGAC  
 DPGFYNLQSGQGCERCDCALGSTNGQCDIRTGQCECQPGITGQHCEVNHFGF  
 GPEGCKPCDCHPEGSLSLQCKDDGRCECREGFVGNRCDQCEENYFYNRSWPGCQE  
 CPACYRLVKDKVADHRVKLQELESILANLGTGDEMVTDAQAFEDRLKEAEREVMDLLRE  
 AQDVKDQNLMDRLQRVNNTLSSQISRLQNIRNTIEETGNLAEQARAHVENTERLIEIA  
 SRELEKAKVAAANVSVTQPESTGDPNNMTLLAEERKLAERHKQEADDIVRVAKTAND



TSTEAYNLLLRTLAGEHQTAFEIEELNRKYEQAKNISQDLEKQAARVHEEAKRAGDKAV  
 EIYASVAQLSPLDSETLENEANNIKMEAENLEQLIDQKLKDYEDLREDMRGKELEVKNLL  
 EKGKTEQQTADQLLARADAALAEAAKKGRTDLQEANDILNNLKDFDRRVNDNKTA  
 AEEALRKIPAINQTITEANEKTREAAQALGSAAADATEAKNKAHEAERIASAVQKNATST  
 KAEAERTFAEVTDLNEVNNMLKQLQEAKEKELKRKQDDADQDMMMMAGMASQAAQEA  
 EINARKAKNSVTSLLSIINDLLEQLGQLDVTDLNKLNEIEGTLNKADEMKVSDLDKRVSD  
 LENEAKKQEAAIMDYNRDIEEIMKDIRNLEDIRKTLPSGCFNTPSIEKP

SEQID No:66

MAAATEHNRPSGDRNLERRCSPNLSREVLVEIFRSLHTLVGQLDLRDDVVKITIDWNK  
 LQSLSAFQPALLFSALEQHILYLQPFLAKLQSPIKEENTTAVEEIGRTEMGNKNEVNDKF  
 SIGDLQEEEEKHKESDLRDVKKTKIHFDPVVQIKAGKAEIDRRISAFIERKQAEINENNVR  
 EFCNVIDCNQENSCARTDAIFTPYPGFKSHVKVSRVVNTYGPQTRPEGIPGSGHKNPS  
 MLRDCGNQAVEERLQNIHAHLRLQTGGPVPRDIYQRIKKLEDKILELEGISPEYFQSVSF  
 SGKRRKVQPPQQNYSLAELDEKISALKQALLRKSREAESMATHLP

SEQID No:67

LCNGVNDGCDNSDESPQQNCRPRTGEENCNVNNGGCAQKCQMVRGAVQCTCHTGY  
 RLTEGHTCQDVNECAEEGYCSQGCTNSEGAFQCWCETGYELRPDRRSCKALGPEP  
 VLLFANRIDIRQVLPHRSEYTLNNLENAIALDFHHRRELFWSDVTDLDRILRANLNGSN  
 VEEVVSTGLESPGGLAVDWVHDKLYWTDSGTSRIEVANLDGAHRKVLLWQNLEKPRAI  
 ALHPMEGTIYWTDWGNTPRIEASSMDGSGRRRIADTHLFWPNGLTIDYAGRRMYWVDA  
 KHHVIERANLDGSHRKAVISQGLPHPFAITVFEDSLYWTDWHTKSINSANKFTGKNQEII  
 RNKLHFPMDIHTLHPQRQPAGKNRCGDNNGGCTHLCLPSGQNYTCACPTGFRKISSH  
 ACAQSLDKFLLFARRMDIRRIISFDTEDLSDDVPLADVRSVAVALDWDSRDDHVYWTDVS  
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 VLIWENLDRPRDIVVEPMGGYMYWTDWGASPKIERAGMDASGRQVISSNLTWPNGLA  
 IDYGSQRLYWADAGMKTIEFAGLDGSKRKVLIGSQLPHPFGLTLYGERIYWTDWQTKSI  
 QSADRLTGLDRETLQENLENLMDIHVFHRRRPPVSTPCAMENGGCASHLCLRSPNPSGF  
 SCTCPTGINLLSDGKTCSPGMNSFLIFARRIDIRMVSLDIPYFADVVPINITMKNTIAVGV  
 DPQEGKVYWSDSTLHRISANLDGSQHEDIITTGLQTTDGLAVDAIGRKVYWTDGTNR  
 IEVGNLDGSMRKVLVWQNLDSPRAIVLYHEMGFMYWTDWGENAKLERSGMDGSDRA  
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 SYIYWTDWQTRSIHRADKGTGSNVILVRSNLPGLMDMQAVDRAQPLGFNKCGRNGG



CSHLCLPRPSGFSCACPTGIQLKGDGKTCDPSPETYLLFSSRGSIRRISLDTSDHTDVHV  
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 ARNLYWTDGTGRNTIEASRLDGSCRKVLINNSLDEPRAIAVFPRKGYLFWTDWGHIAKIER  
 ANLDGSEKVLINTDLGWPNGLTLDYDTRRIYWVDAHLDRIESADLNGKLRQVLVGHVS  
 HPFALTQQDRWIYWTDWQTKSIQRVDKYSGRNKETVLANVEGLMDIIVVSPQRQTGTN  
 ACGVNNGGCTHLCFARASDFVCACPDEPDSQPCSLVPGLVPPAPRATGMSEKSPVLP  
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 LSILLILVVIAALMLYRHKKSFTDPGMGNLTYSNPSYRTSTQEVKIEAIPKPAMYNQLCY  
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SEQID No:68

MRRAPCVRDKLREIVGASTNWRDHVKAMEERKLLHSFLAKSQDGLPPRRMKDSYIEVL  
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 DMCKKSLSPEQDIKFSGHVSWSVGKTSMEVKMQMFQLHGDEFPCVLDATFVMVARDSE  
 NKGPAFVNPLIPESPEEEELFRQGELNKGRRIAFSSTSLKMAPSAEERTTIHEMFLSTL  
 DPKTISFRSRVLPSTNAVWMENSKLKSLEICHPQERNIFNRIFGGFLMRKAYELAWATAC  
 SFGGSRPFVAVDDIMFQKPVEVGSLLFLSSQVCFTQNNYIQVRVHSEVASLQEKQHTT  
 TNVFHFTFMSEKEVPLVFPKTYGESMLYLDGQRHFNSMSGPATLRKDYLVEP

SEQID No:69

MSVKEAGSSGRREQAAYHLHIYPQLSTTESQASCRVTATKDSTTSDVIKDAIASLRDLG  
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 YTYAGSILVAINPFKFLPIYNPKYVKMYENQQLGKLEPHVFALADVAYYTMLRKRVNQCI  
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 RFGKFIQVSYLESGIVRGAVVEKYLLEKSRLVSQEKDERNYHVFYLLLVSEEEERQEF  
 QLKQPEDYFYLNQHNLIKIEDGEDLKHDFERLKQAMEMVGFLPATKKQIFAVLSAILYLG  
 VTYKKRATGREEGLEVGPPPEVLDTLSQLLKVKREILVEVLTKRKTVTVNDKLILPYSLS  
 ITARDSMAKSLYSALFDWIVLRINHALLNKKDVEEAVSCLSIGVLDIFGFEDFERNSEFQF  
 CINYANEQLQYYFNQHIFKLEQEEYQGEGITWHNIGYTDNVGCIHLISKKPTGLFYLLDEE  
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 RPDIVALLRGSDSSYVRELIGMDPVAVFRWAVLRAAIRAMAVLREAGRLRAERA EKAAG  
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PRAFILKSKGIKQKQIIPKNLLDSKSLKLIISMTLHDRTTKSLLHLHKKKKPPSISAQFQTS  
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DEFTRGYTKNDFEPVKQSKAQKKKRKQERAVQEHNGHVFASYQVSIPQSCEQCLSYIW  
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PIVLEKLLEHVEMHGLYTEGLYRKSGAANRTRELRLQALQTDPAAVKLENFPIHAITGVK  
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EEISQLEAAESIAFRRLSLLRQNANKSPKTREPAGGAGRLLTTSRVSPSPSTRNLALGS  
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PPSRSTGMAPLRR

SEQID No:70

MTGERPSTALPDRRWGPRILGFWGGCRVWVFAAIFLLLSLAASWSKAENDFGLVQPLV  
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GSTWSPTAFIVNDGDVPDGLNLGAVVSDVETGVVFLFYSLCAHKAGCQVASTMLVWSK  
DDGVSWSTPRNLSDIGTEVFAPGPGSGIQKQREPRKGRLIVCGHGTLERDGVFCLLS  
DDHGASWRYGSGVSGIPYGQPKQENDFNPDECQPYELPDGSVVINARNQNNYHCHC  
RIVLRSYDACDTLRPRDVTDFPELVDPVVAAGAVVTSSGIVFFSNPAHPEFRVNLTLRW  
SFSNGTSWRKETVQLWPGPSGYSSLATLEGSMDGEEQAPQLYVLYEKGRNHYTESIS  
VAKISVYGTL

SEQID No:71

MAPRLCSISVTARRLLGGPGPRAGDVASAAAARFYSKDNEGSWFRSLFVHKVDPRKDA  
 HSTLLSKKETS NLYKIQFHNVKPEYLDAYNSLTEAVLPKLHLDEDYPCSLVGNWNTWYG  
 EQDQAVHLWRFSGGYPALMDCMNKLKNNKEYLEFRRERSQMILLSRRNQLLLEFSFWN  
 EPQPRMGPNIELRTYKLKPGTMIEWGNNWARAIKYRQENQEAVGGFFSQIGELYVVH  
 HLWAYKDLQSREETR NAAWRKRGWDENVYYTVPLVRHMESRIMIPLKISPLQ

SEQID No:72

MAARVLRARGAAWAGG LLQRAAPCSLLPRLRTWTSSSNRSREDSWLKSLFVRKVDPR  
 KDAHSNLLAKKETS NLYKLQFHNVKPECLEAYNKICQEVLPKIHEDKHYPCTLVGTWNT  
 WYGEQDQAVHLWRYEGGYPALTEVMNKLRENKEFLEFRKARSDMILLSRKNQLLLEFS  
 FWNEPVPRSGPNIELRSYQLRPGTMIEWGNYWARAIRFRQDGNEAVGGFFSQIGQLY  
 MVHHLWAYRDLQTREDIR NAAWHKHGWEELVYYTVPLIQEMESRIMIPLKTSPLQ

SEQID No:73

MGTALLQRGGCFLCLSLLLLGCWAELGSGLEFPGAEGQWTRFPKWNACCESSEMSFQ  
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 RIRRQFRNTTLFIDQVEAKWVEVKSKRRDMTVFSGLFVGGLPPELRAAALKLTLASVRE  
 REPFGKWIRDVRVNSSQVLPVDSGEVKLDDEPPNSGGGSPCEAGEEGEGGVCLNGG  
 VCSVVDDQAVCDCSRTGFRGKDCSQEDNNVEGLAHLMMGDQGKSKGKEEYIATFKG  
 SEYFCYDLSQNPIQSSSDEITLSFKTLQRNGLMLHTGKSADYVNLALKNGAVSLVINLGS  
 GAFEALVEPVNGKFNDNAWHDVKVTRNLRQHSGIGHAMVTISVDGILTTTGYTQEDYT  
 MLGSDDFFYVGGSPSTADLP GSPVSNNFMGCLKEVVYKNNDVRLELSRLAKQGDPKM  
 KIHGVVAFKCENVATLDPITFETPESFISLPKWNAKKTGSISFDFRTTEPNGLILFSHGKP  
 RHQKDAKHPQMIKVDFFAIEMLDGHL YLLLDMSGGTIKIKALLKKVNDGEWYHVDFORD  
 GRSGTISVNTLRTPYTAPGESEILDLDDELYLGGLPENKAGLVFPTEVWTALLNYGYVG  
 CIRDLFIDGQSKDIRQMAEVQSTAGVKPSCSKETAKPCLSNPCKNNGMCRDGWNRYV  
 CDCSGTG YLGRSCEREATVLSYDGSMFMKIQLPVVMHTEAEDVSLRFRSQRAYGILMA  
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 GMAYIDLCKNGDIDYCELNARFGFRNIIADPVTFKTKSSYVALATLQAYTSMHLFFQFKT  
 TSLDGLILYNSGDGND FIVVELVKGYLHYVFDLGNGANLIKSSNKPLNDNQWHNVMIS  
 RDTSNLHTVKIDTKITTQITAGARNLDLKSDLYIGGVAKETYKSLPKLVHAKEGFQGC LAS  
 VDLNGRLPDLISDALFCNGQIERGCEGPSTTCQEDSCSNQGVCLQQWDGFGSCDCSMT

SFSGPLCNDPGTTYIFSKGGGQITYKWPPNDRPSTRADRLAIGFSTVQKEAVLVRVDSS  
 SGLGDYLELHIHQGKIGVKFNVTDDIAIEESNAIINDGKYHVVRFTRSGGNATLQVDSW  
 PVIERYPAGRQLTIFNSQATIIIGGKEQGQPFQGGQLSGLYYNGLKVLNMAAENDANIAIVG  
 NVRLVGEVPSSMTTESTATAMQSEMSTSIMETTTTLATSTARRGKPPTKEPISQTTDDIL  
 VASAECPSDDEDIDPCEPSSGGLANPTRAGGREPYPGSAEVIRESSSTTGMVVGIVAAA  
 ALCILILLYAMYKYRNRDEGSYHVDESRNYISNSAQSNGAVVKEKQPSSAKSSNKNKKN  
 KDKEYYV

SEQID No:74

MTTQQIDLQGGPGPWGFRVLVGGKDFEQPLAISRVTPGSKAALANLCIGDVITAIDGENTS  
 NMTHLEAQNRIGCTDNLTLTVARSEHKVWSPLVTEEGKRHPYKMNLASEPQEV LHIG  
 SAHNRSAMPFTASPASSTTARVITNQYNNPAGLYSSENISNFNNALESKTAASGVEANS  
 RPLDHAQPPSSLVIDKESEVYKMLQEKQELNEPPKQSTSFLVLQEILESEEKGDPNKPS  
 GFRSVKAPVTKVAASIGNAQKLPMCDKCGTGIVGVFVKLRDRHRHPECYVCTDCGTNL  
 KQKGHFFVEDQIYCEKHARERVTPPEGYEYVTVFPK

SEQID No:75

MGAGAETGRGQRAAAPERRHGRLLWLLRGLTLGTAPRRAVRGQAGGGGGPGTAGIVG  
 EAGSLATCELPLAKSEWQKKLTPEQFYVTREKGTPEPPFSGIYLNKEAGMYHCVCCDS  
 PLFSSEKKYCSGTGWPSFSEAHGTSGSDESHTGILRRLDTSLGSARTEVVCKQCEAHL  
 GHVFPDGPNGQRFCINSVALKFKPRKH

SEQID No:76

MTSAAPAKKPYRKAPPEHRELRLLEIPGSRLEQEEPLTDAERMKLLQEENEELRRRLASA  
 TRRTEALERELEIGQDCLELELGQSREELDKFKDKFRRLQNSYASQRTNQELEDKLHT  
 LIKKAEMDRKTL DWEIVELTNKLLDAKNTINKLEELNERYRLDCNPAVQLLKCNKSHFRN  
 HKFADLPCELQDMVRKHLHSGQEAASPGPAPSLAPGAVVPTSVIARVLEKPESLLLNSA  
 QSGSAGRPLAEDVFVHVD MSEGVP GDPASPPAPGSPTPQPNGECHSLGTARGSPEEE  
 LPLPAFEKLN PYPTPSPPHPLYPGRRVIEFSEDKVRIPRNSPLPNCTYATRQAISLSLVEE  
 GSERARPSVPSTPASAQASPHHQPSAPLTL SAPASSASSEEDLLVSWQRAFVD RTP  
 PPAAVAQR TAFGRDALPELQRHFAHSPADRDEVVQAPSARPEESELLLPTEPDSGFPR  
 EEEELNLPISPEEERQSLLPINRGTEEGPGTSHTEGRAWPLPSSSRPQRSPKRMGVHH  
 LHRKDSL TQAQEQGNLLN



SEQID No:77

MGTTASTAQQTVSAGTPFEGQLQGSGTMDSRHSVSIHSFQSTSLHNSKAKSIIPNKVAPV  
 VITYNCKEEFQIHDELLKAHYTLGRLSDNTPEHYLVQGRYFLVRDVTEKMDVLGTVGSC  
 GAPNFRQVQGGLTVFGMGQPSLSGFRRVLQKLQKDGHRECVIFCVREEPVLFLRADE  
 DFVSYTPRDKQNLHENLQGLGPGVRVESLELAIRKEIHDFQAQLSENTYHVYHNTEDLWG  
 EPHAVAIHGEDDLHVTEEVYKRPLFLQPTYRYHRLPLPEQGSPLEAQLDAFVSVLRETP  
 SLLQLRDAHGPPPALVFSCQMVGRTNLGMVLGTLILLHRSGTTSQPEAAPTQAKPLP  
 MEQFQVIQSFLRMVPQGRRMVEEVDRAITACAELHDLKEVVLENQKKLEGIRPESPAQ  
 GSGSRHSVWQRALWSLERYFYLLFNYYLHEQYPLAFALSFSRWLCAHPELYRLPVTLS  
 SAGPVAPRDLIARGSLREDDLVSPDALSTVREMDVANFRRVPRMPIYGTAQPSAKALG  
 SILAYLTDAKRRLRKVVVWSLREEAVLECDGHTYSLRWPGPPVAPDQLETLEAQLKAHL  
 SEPPPGKEGPLTYRFQTCLTMQEVFSQHRRACPGITYHRIPMPDFCAPREEDFDQLE  
 ALRAALSKDPGTGFVFSCLSGQGRTTTAMVVAVLAFWHIQGFPEVGEEELVSVPAKF  
 TKGEFQVVMKVQLLPDGHRVKKEVDAALDTVSETMTPMHYHLREIIICTYRQAKAAKE  
 AQEMRRLQLRSLQYLERYVCLILFNAYLHLEKADSWQRPFSTWMQEVASKAGIYEILNE  
 LGFPELESGEDQPFSRLRYRWQEQSCSLEPSAPEDLL

SEQID No:78

MAALYRPGLRLNWHGLSPLGWPSCRSIQTLRVLSGDLGQLPTGIRDFVEHSARLCQPE  
 GIHICDGTEAENTATLTLEQQGLIRKLPKYNNCWLARTDPKDVARVESKTVIVTPSQRD  
 TVPLPPGGARGQLGNWMSPADFQRAVDERFPGCMQGRTMYVLPFSMGPVGSPLSRI  
 GVQLTDSAYVVASMRIMTRLGTPVLQALGDGDFVKCLHSVGQPLTGQGEPVSQWPCN  
 PEKTLIGHVPDQREIISFGSGYGGNSLLGKKCFALRIASRLARDEGWLAEHMLILGITSPA  
 GKKALCAAFFPSACGKTNLAMMRPALPGWKVECVGDDIAWMRFDSEGRRLRAINPENG  
 FFGVAPGTSATTNPAMATIQSNTIFTNVAETSDGGVYWEGIDQPLPPGVTVTSWLGKP  
 WKPGDKEPCAHPNSRFCAPARQCPIMDPAWEAPEGVPIDAIIFGGRRPKGVPLVYEA  
 NWRHGVFVGRAMRSESTAAAEHKGKIIMHDPFAMRPFFGYNFGHYLEHWLSMEGRKG  
 AQLPRIFHVNWFRRDEAGHFLWPGFGENARVLDWICRRLEGEDSARETPIGLVPKEGA  
 LDLSGLRAIDTTQLFSLPKDFWEQEVDIRSYLTEQVNQDLPKEVLAELEALERRVHKM

SEQID No:79

MLPAATASLLGPLLTAALLPFAQQGQTPNYTRPVFLCGGDVKGESGYVASEGFPNLYP  
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 APLVAPGNQVTLRMTTDEGTGGRGFLLWYSGRATSGTEHQFCGGRLEKAQGTLTTPN

WPESDYPPGISCSWHIIAPPDQVIALTFEKFDLEPDTYCRYDSVSVFNGAVSDDSRRLG  
 KFCGDAVPGSISSEGNELLVQFVSDLSVTADGFSASYKTLPRGTAKEGQGPGPKRGTE  
 PKVKLPPKSQPPEKTEESPSAPDAPTCPKQCRRTGTLQSNFCASSLVVTATVKSMVRE  
 PGEGLAVTVSLIGAYKTGGLDLPSPPTGASLKFYVPCKQCPPMKKGVSYLLMGQVEEN  
 RGPVLPPESFVVLHRPNQDQILTNL SKRK CPSQPVRAAASQD

SEQID No:80

MRMTMEEMKNEAETTS MVSMPLYAVMYPVFNELERVNLSAAQTLRAAFIKA EKENPGL  
 TQDIIMKILEKKSVEVNFTESLLRMAADDVEEYMIERPEPEFQALNEKARALKQILSKIPD  
 EINDRVRFLQTIKDIASAIKELLDTVNNVFKKYQYQNRRALEHQKKEFVKYSKSFSDTLKT  
 YFKDGKAINVFVSANRLIHQTNLILQTFKTVA

SEQID No:81

MTSALTQGLERIPDQLGYLVLSEGAVLASSGDLENDEQAASAISELVSTACGFRLHRGM  
 NVPFKRLSGEPLPLPLVVVLGAGGYFQGLLG FSSSSLLPSPGVSGLATFLPLGLPGIRIV  
 NEKARERRSSRGHSSSNL

SEQID No:82

MGSRDHLFKVLVVGDAAVGKTSLVQRYSQDSFSKHYKSTVGVD FALKVLQWSDYEIVR  
 LQLWDIAGQERFTSMTRLYYRDASACVIMFDVTNATTFSNSQRWKQDLDSKLTLPNGE  
 PVPCLLLANKCDLSPWAVSRDQIDRFSKENGFTGWTETSVKENKNINEAMRV LIEKMM  
 RNSTEDIMSLSTQG DYINLQTKSSSWSCC

SEQID No:83

MAAAKDTHEDHDTSTENTDES NHDPQFEPIVSLPEQEIKTLEED EEEELFKMRAKLFRFA  
 SENDLPEWKERGTDGVKLLKHKEKGAIRLLMRRDKTLKICANH YITPMMELKPNAGSDR  
 AWWNTHADFADEC PKPELLAIRFLNAENAQKF KTKFEECRKEIEEREKKAGSGKNDH  
 AEKVAEKLEALSVKEETKEDAE EKQ

SEQID No:84

MLDSSDSSSQPHWSNELIAEQLQQQVSQ LQDQLDAELEDKRKVLLELSREKAQNEDLK  
 LEVTNILQKHKQEV ELLQNAATISQPPDRQSEPATHPAVLQENTQIEPSEPKNQEEKLS  
 QVLNELQVSHAETTLELEKTRDMLILQRKINVCYQEELEAMMTKADNDNRDHKEKLERL  
 TRLLDLKNNRIKQLEGILRSHDLPTSEQLKDVAYGTRPLSLCLETLP AHGDEDKVDISLLH

QGENLFELHIHQAFLTSAALAQAGDTQPTTFCTYSFYDFETHCTPLSVGPQPLYDFTSQ  
 YVMETDSLFLHYLQEASARLDIHQAMASEHSTLAAGWICFDRVLETVEKVHGLATLIGA  
 GGEEFGVLEYWMRLRFPIKPSLQACNKRKKAQVYLSTDVLGGRKAQEEEFRRSESWEP  
 QNELWIEITKCCGLRSRWLGTQPSPYAVYRFFTFSDHDTAIPASNNPYFRDQARFPVLV  
 TSDLDHYLRREALSIHVFDDEDLEPGSYLGRARVPLLPLAKNESIKGDFNLTDPAEKPNG  
 SIQVQLDWKFPYIPPESEFLKPEAQTKGKDTKDSSKISSEEEKASFPSQDQMASPEVPIEA  
 GQYRSKRKPPHGGGERKEKEHQVVSYSRRKHGKRIGVQGKNRMEYLSLNLNGNTPQQ  
 VNYTEWKFSETNSFIGDGFKNQHEEEEMTLSSHALKQKEPLHPVNDKESSEEQGSEVSE  
 AQTTSDDVIVPPMSQKYPKADSEKMCIEIVSLAFYPEAEVMSDENIKQVYVEYKFYDLP  
 LSETETPVSLRKPRAGEEIHFFHFSKVIDLDPQEQQGRRRFLFDMLNGQDPDQGHKFTV  
 VSDPLDEEKKECEEVGYAYLQLWQILESGRDILEQELDIVSPEDLATPIGRLKVSLQAAA  
 VLHAIYKEMTEDLFS

SEQID No:85

MERSGWARQTFLALLLGATLRARAAAGYYPRFSPFFFLCTHHGELEGDGEQGEVLISL  
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 FGNQFMCSVVASHVSHLPTTNLSFIWIAPPAGTGCVNFMATATHRGQVIFKDALAQQLC  
 EQGAPTDVTVHPLAEIHSDSIILRDDFDSYHQLQLNPNIWVECNNCETGEQCGAIMHG  
 NAVTFCEPYGPRELITTGLNTTASVLQFSIGSGSCRFSYS DPSIIVLYAKNNSADWQLE  
 KIRAPSNVSTIIHILYLPEDAKGENVQFQWKQENLRVGEVYEACWALDNILIINSAHRQVV  
 LEDSLDPVDTGNWLFFPGATVKHSCQSDGNSIYFHGNEGSEFNFATTRDVDLSTEDIQ  
 EQWSEEFESQPTGWDVLGAVIGTECGTIESGLSMVFLKDGERKLCTPSMDTTGYGNLR  
 FYFVMGGICDPGNSHENDIILYAKIEGRKEHITLDTLSYSSYKVPSLVSVVINPELQTPATK  
 FCLRQKNHQGHNRNVWAVDFFHVLPVLPSTMSHMIQFSINLGCGTHQPGNSVSLEFST  
 NHGRSWSLLHTECLPEICAGPHLPSTVYSSENYSGWNRITIPNAALTRNTRIRWRQ  
 TGPILGNMWAIDNVYIGPSCLKFCSGRGQCTRHGCKCDPGFSGPACEMASQTFPMFIS  
 ESFGSSRLSSYHNFYSIRGAEVSFSGCVLASGKALVFNKEGRRQLITSFLDSSQSRFLQ  
 FTLRLGSKSVLSTCRAPDQPGEGVLLHYSYDNGITWKLLEHYSYLSYHEPRIISVELPGD  
 AKQFGIQFRWWQPYHSSQREDVWAIDEIIMTSVLFNSISLDFTNLVEVTQSLGFYLGNV  
 QPYCGHDWTLCFTGDSKLASSMRYVETQSMQIGASYMIQFSLVMGCGQKYTPHMDN  
 QVKLEYSTNHGLTWHLVQEECLPSMPSCQEFTSASIYHASEFTQWRRVIVLLPQKTWS  
 SATRFRWSQSYTAQDEWALDSIYIGQQCPNMCSGHGSCDHGICRCDQGYQGTECH  
 PEAALPSTIMSDFENQNGWESDWQEIVIGGEIVKPEQGGCGVISSGSSLYFSKAGKRQLV  
 SWDLDTSWVDFVQFYIQIGGESASCNKPDSREEGVLLQYSNNGGIQWHLLAEMYFSDF

SKPRFVYLELPAAAKTPCTRFRWWQPVFSGEDYDQWAVDDIILSEKQKQIIPVINPTLP  
QNFYEKPAFDYPMNQMSVWLMLANEGMVKNETFCAATPSAMIFGKSDGDRFAVTRDL  
TLKPGYVLQFKLNIGCANQFSSTAPVLLQYSHDAGMSWFLVKEGCYPASAGKGCEGNS  
RELSEPTMYHTGDFFEWTRITIVIPRSLASSKTRFRRWIQESSSQKNVPPFGLDGVYISEP  
CPSYCSGHGDCISGVCFCDLGYTAAQGTCVSNVPHNEMFDRFEGKLSPLWYKITGA  
QVGTGCGTLNDGKSLYFNPGPKREARTVPLDTRNIRLVQFYIQIGSKTSGITCIKPRTRN  
EGLIVQYSNDNGILWHLLRELD FMSFLEPQIISIDL PQDAKTPATAFRWWQPQH GK HSA  
QWALDDVLIGMNDSSQTGFQDKFDGSIDLQANWYRIQGGQVDIDCLSM D TALIFTENIG  
KPRYAETWDFHVSASTFLQFEMSMGCSKPFSSNSHSVQLQYSLNNGKDWHLVTEECVP  
PTIGCLHYTESSITYTSERFQNWKRITVYLPLSTISPRTRFRRWIQANYTVGADSWAIDNVVL  
ASGCPWMCSGRGICDAGRCVCDRGFGGPYCVPVVPLPSILKDDFN GN LHPDLWPEVY  
GAERGNLNGETIKSGTSLIFKGEGRLMLISRDL DCTNTMYVQFSLRFIAKSTPERSHSILL  
QFSISGGITWHL MDEFYFPQTTNILFINVPLPYTAQTNATRFRLWQPYNNGKKEEIWIVD  
DFIIDGN NVNNPVMLLDTFDFGPREDN WFFYPGGNIGLYCPYSSKGAPEEDS AMVFVS  
NEVGEHSITTRDLNVNENTIIQFEINVGCSTDSSSADPVRLEFSRDFGATWHLLLPLCYH  
SSSHVSSLCSTEHHPSSTYYAGTMQGWRRREV VHFGLHLCG SVRFRWYQGFYPAGS  
QPVTWAIDNVYIGPQCEEMCNGQGSCINGTKCICDPGYSGPTCKISTKNPDFLKDDFEG  
QLESDRFLMSGGKPSRKCGILSSGNNLFFNEDGLRMLMTRDL DLSHARFVQFFMRLG  
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WWQPSENGHFYSPWVIDQILIGGNISGNTVLEDDFTTLD SRKWLLHPGGTKMPVCGST  
GDALVFIEKASTRYVVSTDVAVNEDSFLQIDFAASC SVTDSCYAIELEYSVDLGLSWHPL  
VRDCLPTNVECSRYHLQRILVSDTFNKWTRITLPLPPYTRSQA TRFRWHQPAPFDKQQ  
TWAIDNVYIGDGCIDMCSGHGRCIQGN CVCDEQWGGLYCDDPETS LPTQLKDNFNRA  
PSSQNWLT VNGGKLSTVCGAVASGMALHFSGGCSRL LVTVDLNLTNAEFIQFYFMYGC  
LITPNNRNQGV LLEYSVNGGITWNLLMEIFYDQYSKPGFVNILLPPDAKEIATRFRWWQP  
RHDGLDQNDWAIDNV LISGSADQRTVMLDTFSSAPVPQHERSPADAGPVGRIAFDMFM  
EDKTSVNEHWLFHDDCTVERFCDSPDGVMLCGSHDGREVYAVTHDLTPTEGWIMQFK  
ISVGCKVSEKIAQNQIHVQYSTDFGVSWNYLVPQCLPADPKCSGSVSQPSVFFPTKGW  
KRITYPLPESLVGNPVRFRFYQKYSDMQWAIDNFYLGPGCLDNCRGHGDCLREQCICD  
PGYSGPNCYLTHTLKTF LKERFDSEEIKPDLWMSLEGGSTCTECGILAEDTALYFGGST  
VRQAVTQDLDLRGAKFLQYWGRIGSENNMTSCHRPICRKEGVLLDYSTDGGITWTLLH  
EMDYQKYISVRHDYILLPEDALTNTTRLRWWQPFVISNGIVVSGVERAQWALDNILIGGA  
EINPSQLVDTFDDEGTSHEENWSFYPNAVRTAGFCGNPSFHL YWPNKKKDKTHNALSS  
RELIIQPGYMMQFKIVVGCEATSCGDLHSVMLEYTKDARS DSWQLVQTQCLPSSSNSIG



CSPFQFHEATIYNSVNSSSWKRITQLPDHVSSSATQFRWIKGEETEKQSWAIDHVIYIG  
 EACPKLCSGHGYCTTGAICICDESFGGDDCSVFSHDLPSYIKDNFESARVTEANWETIQ  
 GGVIGSGCGQLAPYAHGDSLYFNGCQIRQAATKPLDLTRASKIMFVLQIGSMSQTDSCN  
 SDLSGPHAVDKAVLLQYSVNNGITWHVIAQHQPkdftQAQRVSYNVPLEARMKGVLLR  
 WWQPRHNGTGHDQWALDHVEVVLVSTRKQNYMMNFSRQHGLRHFYNRRRRSLRRY  
 P

SEQID No:86

MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQL  
 ERIEEMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVA  
 SQPARVVDEREQMAISGGFIRRVTDARENEMDENLEQVSGIIGNLRHMALDMGNEIDT  
 QNRQIDRIMEKADSNKTRIDEANQRATKMLGSG

SEQID No:87

MASTISAYKEKMKELSVLSLICSCFYTQPHPNTVYQYGDMEVKQLDKRASGQSFEVILK  
 SPDLSPESPMLSSPPKKKDTSLLELQKRLEAAEERRKTQEAQVLKQLAERREHEREV  
 LHKALEENNNFSRQAEKLNKYMELSKEREHLAALRERLREKELHAAEVRRNKEQRE  
 MSG

SEQID No:88

MKDRTQELRTAKDSDDDDDDVAVTVDRDRFMDEFFEQVEEIRGFIDKIAENVEEVKRKHS  
 AILASPNPDEKTKEELEELMSDIKKTANKVRSKLKSIEQSIEQEEGLNRSSADLRIRKTQH  
 STLSRKFEVVMSEYNATQSDYRERCKGRIQRQLEITGRTTTSEELEDMLESGNPAIFAS  
 GIIMDSSISKQALSEIETRHSEIIKLENSIRELHDMFMDMAMLVESQGEMIDRIEYNVEHAV  
 DYVERAVSDTKKAVKYQSKARRKKIMIIICCVILGIVIASTVGGIFA

SEQID No:89

MAASMFYGRLVAVATLRNHRPRTAQRAAAQVLGSSGLFNNHGLQVQQQQQRNLSLHE  
 YMSMELLQEAGVSVPKGYYVAKSPDEAYAIKKLGSKDVVIAQVLAGGRGKGTFESGL  
 KGGVKIVFSPEEAKAVSSQMIGKKLFTKQTGEKGRICNQLVCERKYPRREYYFAITME  
 RSFQGPVLIGSSHGGVNIEDVAAETPEAIIKEPIDIEEGIKKEQALQLAQKMGFPPNIVESA  
 AENMVKLYSLFLKYDATMIEINPMVEDSDGAVLCMDAKINFDSNSAYRQKKIFDLQDWT  
 QEDERDKDAAKANLNYIGLDGNIGCLVNGAGLAMATMDIIKLHGGTPANFLDVGGGATV

HQVTEAFKLITSDKKVLAILVNIFGGIMRCDVIAQGIVMAVKDLEIKIPVVVRLQGTRVDDA  
KALIADSGLKILACDDLDEAARMVVKLSEIVTLAKQAHVDVKFQLPI

SEQID No:90

MAPLDLDKYVEIARLCKYLPENDLKRLCDYVCDLLEESNVQPVSTPVTVCGDIHGQFY  
DLCELFRTGGQVPDTNYIFMGDFVDRGYYSLETFTYLLALKAKWPDRITLLRGNHESRQ  
ITQVYGFYDECQTKYGNANAWRYCTKVFDMLTVAALIDEQILCVHGGGLSPDIKTLDQIRTI  
ERNQEIPHKGAFCDLVWSDPEDVDTWASPRGAGWLFGAKVTNEFVHINNKLICRAH  
QLVHEGYKFMFDEKLVTVWSAPNYCYRCGNIASIMVFKDVNTREPKLFRAVPDSERVIP  
PRTTTPYFL

SEQID No:91

MATRSSRRESRLPFLFTLVALLPPGALCEVWTQRLHGGSAPLPQDRGFLVVQGDPREL  
RLWARGDARGASRADEKPLRRKRSAALQPEPIKVYGGVSLNDSHNQMVVHWAGEKS  
NVIVALARDSLALARPSSDVYVSYDYGKSFKKISDKLNFGGLGNRSEAVIAQFYHSPADN  
KRYIFADAYAQYLWITFDFCNTLQGFSIPFRAADLLLHASKASNLLGFDRSHPNKQLWKS  
DDFGQTWIMIQEHVKSFSWGIDPYDKPNTIYIERHEPSGYSTVFRSTDFQSSRENQEVIL  
EEVRDFQLRDKYMFATKVVHLLGSEQQSSVQLWVSFGRKPMRAAQFVTRHPINEYYIA  
DASEDQVFVVCVSHSNNRTNLYISEAEGLKFSLSLENVLYYSPGGAGSDTLVRYFANEFP  
ADFHRVEGLQGVYIATLINGSMNEENMRSVITFDKGGTWEFLQAPAFTGYGEKINCELS  
QGCSHLAQRLSQLLNQLRRMPILSKESAPGLIATGSVGKNLASKTNVYISSAGARW  
REALPGPHYTWGDHGGIITAIAAQGMETNELKYSTNEGETWKTFIFSEKPVFVYGLLTEP  
GEKSTVFTIFGSNKENVHSWLILQVNATDALGVPCTENDYKLWSPSDERGNECLLGHK  
TVFKRRTPHATCFNGEDFDRPVVVSNCSCCTREDYECDFGFKMSEDLSLEVCVPDPEFS  
GKSYSPVPCPVGSTYRRTRGYRKISGDTCSGGDVEARLEGELVPCPLAEENEFILYAV  
RKSIYRYDLASGATEQLPLTGLRAAVALDFDYEHNCLYWSDLALDVIQRLCLNGSTGQE  
VIINSGLETVEALAFEPLSQLLYWVDAGFKKIEVANPDGDFRLTIVNSSVLDRPRALVLP  
QEGVMFWTDWGDLPKGIYRSNMDGSAAYHLVSEDVKWPNGISVDDQWIYWTDAYLE  
CIERITFSGQQRSVILDNLPHPYAIAVFKNEIYWDDWSQLSIFRASKYSGSQMEILANQLT  
GLMDMKIFYKGKNTGSNACVPRPCSLCLPKANNRSRSCRCPEDVSSSVLPSPGDLMCD  
CPQGYQLKNNTCVKEENTCLRNQYRCSNGNCINSIWWCDFDNDCGDMSDERNCPTTI  
CDLDTQFRCQESGTCIPLSYKCDLEDDCGDNSDESHCEMHQCRSDEYNCSGMCIRS  
SWVCDGDNDCRDWSDEANCTAIYHTCEASNQCRNGHCIPQRWACDGDGTDGQDGS  
DEDPVNCEKKCNGFRCPNGTCIPSSKHCDGLRDCSDGSDEQHCEPLCTHFMDFVCKN

RQQCLFHSMVCDGIIQCRDGSDEDAAFAGCSQDPEFHKVCDEFGFQCQNGVCISLIWK  
 CDGMDDCGDYSDEANCENPTEAPNCSRYFQFRCENGHCIPNRWKCDREND CGDWS  
 DEKDCGDSHILPFSTPGPSTCLPNYYRCSSGTCVMDTWVCDGYRDCADGSDEEACPL  
 LANVTAASTPTQLGRCDRFEFECHQPKTCIPNWKRCDCGHQDCQDGRDEANCPTHSTL  
 TCMSREFQCEDGEACIVLSERCDGFLDCSDESDEKACSDELTVYKVQNLQWTADFSG  
 DVTLTWMRPKKMPSASCVYNVYYRVVGESIWKLETHSNKTNVTLKVLKPDTTYQVKV  
 QVQCLSKAHNTNDFVTLRTPEGLPDAPRNLQLSLPREAEGVIVGHWAPPIHTHGLIREYI  
 VEYSRSGSKMWASQRAASNFT EIKNLLVNTLYTVRVA AVTSRGIGNWSDSKSITTIK GK  
 VIPPPDIHIDSYGENYLSFTLT MESDIKVNGYVVNLFWAFDTHKQERRTLNFRGSILSHKV  
 GNLT AHTSYEISAWAKTDLGDSPLAFEHVMTRGVRPPAPSLKAKAINQTAVECTWTGP  
 RNVVYGIFYATSFLDLYRNP KSLTTSLHNKTVIVSKDEQYLFLVRVVVPYQGPSSDYVVV  
 KMIPDSRLPPRHLHVHTGKTSVVIKWESPYDSPDQDLLYAI AVKDLIRKTD RSYKV KSR  
 NSTVEYTLNKLEPGGKYHII VQLGNMSKDSSIKITTVSLSAPDALKIITENDHVLLFWKSLA  
 LKEKHFNESRGYEIHMFD SAMNITAYLGNTTDNFFKISNLKMGHNYTFTVQARCLFGNQI  
 CGEPAILLYDELGSGADASATQAARSTDVA AVVVPILFLILLSLGVGFAILYTKHRRLOSS  
 FTA FANSHYSSRLGSAIFSSGDDLGEDDEDAPMITGFSDDVPMVIA

SEQID No:92

MEGASFGAGRAGAALDPVSFARRPQTLLRVASWVFSIAVFGPIVNEGYVNTDSGP ELR  
 CVFNGNAGACRFGVALGLGAFLACAAFLLLDVRFQQISSVRDRRRRAVLLDLGFSGLWS  
 FLWFGFCFLT NQWQRTAPGPATTQAGDAARAAIAFSFFSILSWVALTVKALQRFRLGT  
 DMSLFATEQLSTGASQAYPGYPVGSGVEGTETYQSPPTETLDTSPKGYQVPAY

SEQID No:93

MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAE E  
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 NPREPAVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELST  
 EEEIHHFKNESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQH SALTRLR  
 LRNVFRRFLRDFQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAE GEP  
 YIRDSGVAPTDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQ  
 ASLFGKKAKAHKAFGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSL  
 PSRAAALS FVSLVDGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLEPFVQAKLRPE  
 DGLYLIHWSTSHPYRLILTVAQRSQAPDGMQSLRLRKFP IEQQDGAFVLEGWGRSFPS  
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DQKEITQLSHLGQGTRTNVYEGRLRVEGSGDPEEGKMDDDEDPLVPGRDRGQELRVVL  
 KVLDP SHHDIALAFYETASLMSQVSHTHLAFVHGVCVRGPENSMVTEYVEHGPLDVWL  
 RRERGHVPMWKMVVAQQLASALSYLENKNLVHGNVCGRNILLARLG LAEGTSPFIKL  
 SDPGVGLGALSREERVERIPWLAPECLPGGANSLSAMDKWGFGATLLEICFDGEAPL  
 QSRSPSEKEHFYQRQHRLPEPSCPQLATLTSQCLTYEPTQRPSFRTLRLDLTRVQPHNL  
 ADVLTVNRDSPA VGPTTFHKRYLKKIRDLGEGHFGKVS LYCYDPTNDGTGEMVAVKAL  
 KADCGPQHRSGWKQEIDILRTLYHEHIIKYKGCCEDQGEKSLQLVMEYVPLGSLRDYLP  
 RHSIGLAQLLLFAQQICEGMAYLHAHDYIHRDLAARNVLLDNDRLVKIGDFGLAKAVPEG  
 HEYYRVREDGDSPVFWYAPECLKEYKFYYASDVWSFGVTLYELLTHCDSSQSPPTKFL  
 ELIGIAQGQMTVLRLTELLERGERLPRPDKCPCEVYHLMKNCWETEASFRPTFENLIPIL  
 KTVHEKYQQGQAPSVFSVC

SEQID No:94

MVLIWRRSRYLLREIEAQWSISALWEGFQKWRDNLFLQIVQLIQHVYSVWTASRTVFIKII  
 VTRHTSTGGGFCDCGDTEAWKTGPFCVNHEPGRAGTIKENSRCPLNEEVIVQARKIFP  
 SVIKYV VEMTIWEEEEKELPPELQIREKNERYCYVLFNDEHHSYDHVIYSLQRALDCELA  
 AQLHTTAIDKEGRRAVKAGAYAACQEAKEDIKSHSENVSQHPLHVEVLHSEIMAHQKFA  
 LRLGSWMNKIMSYSSDFRQIFCQACLREEPDSENPC LISRLMLWDAKLYKGARKILHELI  
 FSSFFMEMEYKKLFAMEFVKYYKQLQKEYISDDHDRSISITALSVQMFTVPTLARHLIEE  
 QNVISVITETLLEVLPEYLDRNNKFNFGQYSQDKLGRVYAVICDLKYILISKPTIWTERLR  
 MQFLEGFRSFLKILTCMQGMEEIRRQVGQHIEVDPDWEAAIAIQMQLKNILLMFQEWCA  
 CDEELLVAYKECHKAVMRCSTSFISSSKT VVQSCGHSLET KSYRVSEDLVSIHLPLSRT  
 LAGLHVRLSRLGAVSRLHEFVSFEDFQVEVLVEYPLRCLVLVAQVVAEMWRRNGLSLIS  
 QVFYYQDVKCREEMYDKDIIMLQIGASLMDPNKFLLLVLQRYELAEAFNKTISTKDQDLIK  
 QYNTLIEEMLQVLIYIVGERYVPGVGNVTKEEVTMREIIHLLCIEPMPHSAIAKNLPEN

SEQID No:95

MKALRLSASALFCLLLINGLGAAPPGRPEAQPPPLSSEHKEPVAGDAVP GPKDGSAP EV  
 RGARNSEPQDEGELFQGVDPRALAAVLLQALDRPASPPAPSGSQQGPEEEAAEALLTE  
 TVRSQTHSLPAAGEPEPAAPPRPQTPENGPEASDPSEELEALASLLQELRDFSPSSAK  
 RQQETAAAETETRTHTLTRVNLESPGPERVWRASWGEFQARVPERAPLPPPAPSQFQ  
 ARMPDSGPLPETHKFGEGVSSPKTHLGEALAPLSKAYQGVAAPFPKARRAESALLGGS  
 EAGERLLQQGLAQVEAGRRQAEATRQAAAQEERLADLASDLLLQYLLQGGARQRGLG  
 GRGLQEAAEERESAREEEEEAEQERRGGEERVGEEDEEAAEAAEAEADEAERARQNAL



LFAEEEDGEAGAEDKRSQEETPGHRRKEAEGTEEGGEEEDDEEMDPQTIDSLIELSTK  
 LHLPADDVVSIIEVEEKRNRRKKAPPEPVPPPRAAPATHVRSPQPPPPPPSARDELP  
 DWNEVLPPWDREEDDEVYPPGPYHPFPNYIRPRTLQPPSALRRRRHYHHALPPSRHYPG  
 REAQARHAQQEEAEAEERRLQEQUEELENYIEHVLLRRP

SEQID No:96

MAHRKLESVGSGMLDHRVRPGPVPHSQEPESDMELPLEGYVPEGLELAALRPESPA  
 PEEQECHNHSPDGDSSSDYVNNTSEEEDYDEGLPEEEEGITYYIRYCPEDDSYLEGMD  
 CNGEEYLAHSAHPVDTDECQEAVEEWTDGAGPHPHGHEAEGSQDYPDGQLPIPEDEP  
 SVLEAHDQEEDGHYCASKEGYQDYYPEEANGNTGASPYRLRRGDGDLEDQEEDIDQI  
 VAEIKMSLSMTSITSASEASPEHGPEPGPEDSVEACPPIKASCSPSRHEARPKSLNLLPE  
 AKHPGDPQRGFKPKTRTPEERLKWPHQVCNGLEQPRKQQRSDLNGPVDNNNIPETK  
 KVASFPSFVAVPGPCEPEDLIDGIIFAANYLGSTQLLSERNPSKNIRMMQAEAVSRVKR  
 MQKAAKIKKKANSEGDAQTLTEVDLFISTQRIKVLNADTQETMMDHALRTISYIADIGNIV  
 VLMARRRMPRSASQDCIETTPGAQEGKKQYKMICHVFESDAQLIAQSIGQAFSVAYQ  
 EFLRANGINPEDLSQKEYSDIINTQEMYNDLIHFSNSENCKELQLEKHKGEILGVVVVE  
 SGWGSILPTVILANMMNGGPAARSGKLSIGDQIMSINGTSLVGLPLATCQGIIKGLKNQT  
 QVKLNIVSCPPVTTVLIKRPDLKYQLGFSVQNGIICSLMRGGIAERGGVRVGHRIIEINGQ  
 SVVATAHEKIVQALSNSVGEIHMKTMPAAMFRLLTGQETPLYI

SEQID No:97

MDTSSVGLELTDQTPVLLGSTAMATSLTNVGNSFSGPANPLVSRSNKFQNSSVEDDD  
 DVVFIQVQPPPPSVPVVADQRTITFTSSKNEELQGNDKITPSSKELASQKGSVSETIVI  
 DDEEDMETNQGQEKNSNFIERRPPETKNRTNDVDFSTSSFSRSKVNAGMGNNGITTE  
 PDSEIQIANVTTLETGVSSVNDGQLENTDGRDMNLMITHVTSLQNTNLGDVSNGLQSSN  
 FGVNIQTYTPSLTSQTKTGVPFNPGRMNVAGDVFQNGESATHHNPDSWISQSASFPR  
 NQKQPGVDSLSPVASLPKQIFQPSVQQQPTKPVKVTANCKKPLQKGQTAYQRKGS  
 HLFCSTTCLSSFSHKPAPKKLCVMCKKDITTMKGTIVAQVDSSESFQEFCTSCLSLYED  
 KQNPTKGALNKSRICTICGKLTEIRHEVSFKNMTHKLCSDHCFNRYRMANGLIMNCCEQ  
 CGEYLPSKGAGNNVLVIDGQQKRFCCQSCVSEYKQVGSHPSFLKEVRDHMQDSFLMQ  
 PEKYGKLTCTGCRTOCRFFDMTQCIGPNGYMEPYCSTACMNSHKTKYAKSQSLGIIC  
 HFCKRNSLPQYQATMPDGKLYNFCNSSCVAKFQALSMQSSPNGQFVAPSDIQLKCN  
 CKNSFCCKPEILEWENKVHQFCKTCSDDYKKLHCIVTYCEYCQEEKTLHETVNFSGVK  
 RPFCSSEGCKLLYKQDFARRLGLRCVTCNYCSQLCKKGATKELDGVVRDFCSEDCKKF

QDWYYKAARCDCCCKSQGTLKERVQWRGEMKHFCDQHCLLRFYCQQNEPNMTTQKG  
 PENLHYDQGCQTSRTKMTGSAPPPSPTPNKEMKNKAVLCKPLTMTKATYCKPHMQTK  
 SCQTDDTWRTYVPVPIPVVYIPVPMHMYSQNIPVPTTVPVVPVVPVFLPAPLDSSEKI  
 PAAIEELKSKVSSDALDTELLTMTDMMSEDEGKTETTNINSVIIETDIIGSDLLKNSDPETQ  
 SSMPDVPYEPDLIDIEIDFPRAAEELDMENEFLLPPVFGEEYEEQPRPRSKKKKGAKRKAV  
 SGYQSHDDSSDNSECSFPFKYTYGVNAWKHWVKTRQLDEDLLVLDELKSSKSVKLKE  
 DLLSHTTAELNYGLAHFVNEIRRPNGENYAPDSIYYLCLGIQEYLCGSNRKDNIFIDPGY  
 QTFEQELNKILRSWQPSILPDGSIFSRVEEDYLWRIKQLGSHSPVALLNTLFYFNTKYFG  
 LKTVEQHLRLSFGTVFRHWKKNPLTMENKACLRYQVSSLCGTDNEDKITTGKRKHEDD  
 EPVFEQIENTANPSRCPVKMFECYLSKSPQNLNQRMDVFYQLQPECSSSTDSPVWYTST  
 SLDRNTLENMLVRVLLVKDIYDKDNYELDEDTD

SEQID No:98

MARHVFLTGPPGVGKTTLIHKASEVLKSSGVPVDGFYTEEVRQGGRRIGFDVVTLSGTR  
 GPLSRVGLEPPPGBKRECRVGQYVVDLTSFEQLALPVLRNADCSSGPGQRVCVIDEIGK  
 MELFSQLFIQAVRQTLSTPGTILGTIPVPKGKPLALVEEIRNRKDVKVFNVTKENRNHLL  
 PDIVTCVQSSRK

SEQID No:99

MAAPPEPGEPEERKSLKLLGFLDVENTPCARHSILYGSLGSVVAGFGHFLFTSRIRRS  
 DVGVGGFILVTLGCWFHCRYNYAKQRIQERIAREEIKKKILYEGTHLDPERKHNGSSSN

SEQID No:100

MLSLDFLDDVRRMNKRQLYYQVLNFGMIVSSALMIWKGLMVITGSESPIVVVLSGSMEP  
 AFHRGDLLFLTNRVEDPIRVGEIVVFRIEGREIPIVHRVLKIHEKQNGHIKFLTNGDNNVD  
 DRGLYKQGQHWLEKKDVVGRARGFVPYIGIVTILMNDYPKFYAVLFLGLFVLVHRE

SEQID

No:101AESDLQLAQIKCNLGRAVQLQELWPGGLFWTRKLSTYIRLYGRKFSKEDHVLFK  
 LLYELVSIPKLEISM MQGFARLLINLLKKKELLSRADLELPWRPLYDMVERILYSKTEHLG  
 LNWFPSNVENILKTLVKSCRPYFPADATAEMLEEWRLMCPFDVTMQKAITYFEIFLPTS  
 LPPELHHKGFKLWFDELIGLWVSVQNL PQWEGQLVNLFARLATDNIGYIDWDPYVPKIF  
 TRILRSLNLPVGSSQVLVPRFLT NAYDIGHAVIWITAMMGGPSKLVQKHLA GLFNSITSFY  
 HPSNNGRWLNKLMKLLQRLPNSVVRRLHRERYKKPSWLTPVPDSHKLTDQDVTDFVQ

CIIQPVLLAMFSKTGSLEAAQALQNLALMRPELVIPPVLERTYPAETLTTEPHQLTATLSC  
 VIGVARSLVSGGRWFPEGPHTHMLPLLMRALPGVDPNDFSKCMITFQFIATFSTLVPLVD  
 CSSVLQERNDLTEVERELCSATAEFEDFVLQFMDRCFGLIESSTLEQTREETETETKMT  
 LESLVELGLSSTFSTILTQCSKEIFMVALQKVFNFSTSHIFETRVAGRMVADMCRAAVKC  
 CPEESLKLFPVPHCCSVITQLTMNDDVLNDEELDKELLWNLQLLSEITRVDGRKLLLYREQ  
 LVKILQRTLHLTCKQGYTLSCNLLHLLRSTTLIYPTEYCSVPGGFDKPPSEYFPIKDWG  
 KPGDLWNLGIQWHVPSSEEVSFAYLLDSFLQPELVKLQHCGDGKLEMSRDDILQSLTI  
 VHNCLIGSGNLLPPLKGEPVTNLVPSMVSLEETKLYTGLEYDLSRENHREVIATVIRKLLN  
 HILDNSEDDTKSLFLIKIIGDLLQFQGSHKHEFDSRWKSFNLVKKSMENRLHGKKQHARA  
 LLIDRVMLQHELRTLTVEGCEYKKIHQDMIRDLLRLSTSSYSQVRNKAQQTFFAALGAYN  
 FCCRDIIPLVLEFLRPDRQGVTQQQFKGALYCLLGNHSGVCLANLHDWDCIVQTWPAIV  
 SSGLSQAMSLEKPSIVRLFDDLAEKIHRQYETIGLDFTIPKSCVEIAELLQQSKNPSINQIL  
 LSPEKIKEGIKRQQEKNADALRNYENLVDTLLDGVEQRNLPWKFEHIGIGLLSLLLRDDR  
 VLPLRAIRFFVENLNHDAIVVRKMAISAVAGILKQLKRTHKKLTINPCEISGCPKPTQIIAGD  
 RPDNHWLHYDSKTIPRTKKEWESSCFVEKTHWGYTWPKNMVVYAGVEEQPKLGRS  
 REDMTEAEQIIFDHFSDPKFVEQLITFLSLEDKRGKDKFNPRRFCLFKGIFRNFDDAFLPV  
 LKPHLEHLVADSHESTQRCVAEIIAGLIRGSKHWTFEKVEKLWELLCPLLRTALSNTIVET  
 YNDWGACIATSCESRDPRKLHWLFELLLESPLSGEGGSFVDACRLYVLQGGGLAQGEW  
 RVPELLHRLKYLEPKLTQVYKNVRERIGSVLTYIFMIDVSLPNTTPTISPHVPEFTARILE  
 KKLPLMDVDEEIQNHVMEENGIGEEDERTQGILLKTLKWLMAAGRSFSTAVTEQLQL  
 LPLFFKIAPVENDNSYDELKRDAKLCLSLMSQGLLYPHQVPLVLQVLKQTARSSSWHAR  
 YTVLTYLQTMVFYNLFIFLNNEDAVKDIRWLVISLLEDEQLEVREMAATTLSGLLQCNFLT  
 MDSPMQIHFEQLCKTKLPKKRKRDPGSGVGDTPSAELVKRHAGVLGLGACVLSSPYDV  
 PTWMPQLLMNLSAHLNDPQPIEMTVKKTLNFRRTHHDNWQEHKQQFTDDQLLVLTDL  
 LVSPCYA

SEQID No:102

MSDSVILRSIKKFGEENDGFESDKSYNNDDKKSRLQDEKKGDGVRVGFFQLFRFSSSTDI  
 WLMFVGSLSLCAFLHGIAQPGVLLIFGTMTDVFIDYDVELQELQIPGKACVNNTIVWTNSSL  
 NQNMTNGTRCGLLNIESEMIKFASYAGIAVAVLITGYIQICFWVIAAARQIQKMRKFYFR  
 RIMRMEIGWFDCNSVGELNTRFSDDINKINDAIADQMALFIQRMTSTICGFLLGFFRGWK  
 LTLVIISVSPLIGIGAATIGLSVSKFTDYELKAYAKAGVVADEVISSMRTVAAFGGGEKREVE  
 RYEKNLVFAQRWGIRKGIVMGFFTGFVWCLIFLCYAVAFWYGSTLVLDEGEYTPGTLVQ  
 IFLSVIVGALNLGNASPCLEAFATGRAAATSIFETIDRKPIIDCMSEDGYKLDRIKGEIEFHN

VTFHYPSRPEVKILNDLNMVIKPGEMTALVGPSGAGKSTALQLIQRFYDPCEGMVTVDG  
 HDIRSLNIQWLRDQIGIVEQEPVLFSTTIAENIRYGRE DATMEDIVQAAKEANAYNFIMDL  
 PQQFDTLVGEGGGQMSGGQKQRVAIARALIRNPKILLDMATSALDNESEAMVQEVLS  
 KIQHGHTIISVAHRLSTVRAADTIIGFEHGTAVERGTHEELLERKGVYFTLVTLQSQGNQA  
 LNEEDIKDATEDDMLARTFSRGSYQDSL RASIRQRSKSQLSYLVHEPPLAVVDHKSTYE  
 EDRKDKDIPVQEEVEPAPVRRILKFSAPWPYMLVGSGVGA AVNGTVTPLYAFLFSQILG  
 TFSIPDKEEQRSQINGVCLLFVAMGCVSLFTQFLQGYAFAKSGELLTKRLRKFGFRAML  
 GQDIAWFDDLNRNSPGALTTRLATDASQVQGAAGSQIGMIVNSFTNVTVMIIAFSFSWK  
 LSLVILCFFPFLALSGATQTRMLTG FASRDKQALEMVGQITNEALSNI RTVAGIGKERRFI  
 EALETELEKPFKTAIQKANIYGFCFAFAQCIMFIANSASYRYGGYLISNEGLHFSYVFRVIS  
 AVVLSATALGRAFSYTPSYAKAKISAARFFQLLDRQPPISVYNTAGEKWDNFQGKIDFVD  
 CKFTYPSRPDSQVLNGLSVSISPGQTLAFVGSSGCGKSTS IQLLERFYDPDQGKVMIDG  
 HDSKKVNVQFLRSNIGIVSQEPVLFACSIMDNIKYGDNTKEIPMERVIAAAKQAQLHDFV  
 MSLPEKYETNVGSQGSQLSRGEKQRIAIARAIVRDPKILLLDEATSALDTESEKTVQVAL  
 DKAREGRTCIVIAHRLSTIQNADI IAVMAQGVVIEKGTHEELMAQKGAYYKLVTTGSPIS

SEQID No:103

MSLVLNDLLICCRQLEHDRATERKKEVEKFKRLIRDPETIKHLDRHSDSKQGKYLNWDA  
 VFRFLQKYIQKETEC LRIAKPNVSASTQASRQKKMQEISSLVKYFIKCANRRAPRLKCQE  
 LLNYIMDTVKDSSNGAIYGADCSNILLKDILSVRKYWCEISQQQWLELFSVYFRLYLKPS  
 QDVHRVLVARIIHAVTKGCCSQT DGLNSKFLDFFSKAIQCARQEKSSSGLNHILAALTIFL  
 KTLAVNFRI RVCELGD EILPTLLYIWTQHRLNDSLKEVIIELFQLQIYIHHPKGAKTQEKGA  
 YESTKWRSILYNLYDLLVNEISHIGSRGKYSSGFRNIAVKENLIELMADICHQVFNEDTRS  
 LEISQSYTTTQRESSDYSVPCKRKKIELGWEVIKDHLQKSQND FDLVPWLQIATQLISKY  
 PASLPNCELSPLL MILSQLLPQQRHGERTPYVLRCLTEVALCQDKRSNLESSQKSDLLK  
 LWNKIWCITFRGISSEQIQAENFGLLGAI IQGSLVEVDREFWKLF TGSACRPSCPAVCCL  
 TLALTTSIVPGAVKMGIEQNMCEVNRSFSLKESIMKWLLFYQLEGDLENSTEVPPI LHSN  
 FPHLVLEKILVSLTMKNCKAAMNFFQSVPECEHHQKDKEELSFSEVEELFLQTTFDKMD  
 FLTIVRECGIEKHQSSIGFSVHQNLKESLDRCLLGLSEQLLNNYSSEITNSETLVRC SRLL  
 VGVLGCCYCYMGVIAEEEEAYKSELFQKANS LMQCAGESITLFKNKTNEEFRI GSLRNMMQ  
 LCTRCLSNCTKKSPNKIASGFFLRLLTSKLMNDIADICKSLASF IKKPFDRGEVESMEDDT  
 NGNLMEVEDQSSMNL FNDYPDSSVSDANEPGESQSTIGAINPLAEEYLSKQDLLFLDML  
 KFLCLCVTTAQTNTVSFRAADIRRKLLMLIDSSTLEPTKSLHLHMYLMLLKELPGEEYPLP  
 MEDVLELLKPLSNVCSLYRRDQDVCKTILNHVLHVVKNLGQSNMDSENTRDAQQGQFLT



VIGAFWHLTKERKYIFSVRMALVNCLKTLLEADPYSKWAILNVMGKDFPVNEVFTQFLAD  
 NHHQVRMLAAESINRLFQDTKGDSSRLLKALPLKLQQTAFENAYLKAQEGMREMSHSA  
 ENPETLDEIYNRKSVLLTLIAVVLSCSPICEKQALFALCKSVKENGLEPHLVKKVLEKVSE  
 TFGYRRLEDFMASHLDYLVLEWLNLDQTEYNLSSFPFILLNYTNIEDFYRSCYKVLIPHLV  
 IRSHFDEVKSIANQIQEDWKSLLTDCFPKILVNILPYFAYEGTRDSGMAQQRETATKVYD  
 MLKSENLLGKQIDHLFISNLPEIVVELLMTLHEPANSSASQSTDLCDFSGDLDPAPNPPH  
 FPSHVIKATFAYISNCHKTKLKSILEILSKSPDSYQKILLACEQAAETNNVYKKHRILKIYHL  
 FVSLLLKDIKSGLGGAFAFVLRDVIYTLIHYINQRPSCIMDVSLRSFSLCCDLLSQVCQTA  
 VTYCKDALENHLHVIVGTLIPLVYEQVEVQKQVLDLLKYLVIDNKNENLYITIKLLDPFPD  
 HVVFKDLRITQQKIKYSRGPFSLLEEINHFLSVSVYDALPLTRLEGLKDLRRQLELHKDQ  
 MVDIMRASQDNPQDGIMVKLVVNLLQLSKMAINHTGEKEVLEAVGSCLEGEVGPIDFSTIA  
 IQHSDKASYTKALKLFEDKELQWTFIMLTYNNTLVEDCVKVRSAAVTCLKNILATKTGH  
 SFWEIYKMTTDPMLAYLQPFRTSRKKFLEVPRFDKENPFEGLDLNLWIPLSENHDIWIK  
 TLTCAFLDSGGTKCEILQLLKPMCEVKTDFCQTVLPYLIHDILLQDTNESWRNLLSTHVQ  
 GFFTSCLRHFSQTSRSTTPANLDSESEHFFRCCLDKKSQRTMLAVVDYMRQKRPSS  
 GTIFNDAFWLDLNYLEVAKVAQSCAAHFTALLYAEIYADKKSMDDQEKRSALAFEEGSQS  
 TTISSLSEKSKEETGISLQDLLLEIYRSIGEPDSLYGCGGGKMLQPITRLRTEHEAMWG  
 KALVTYDLETAIPSSTRQAGIIQALQNLGLCHILSVYLGKLDYENKDWCPLEELHYQAA  
 WRNMQWDHCTSVSKEVEGTSYHESLYNALQSLRDREFSTFYESLKYARVKEVEEMCK  
 RSLESVYSLYPTLSRLQAIGELESIGELFSRSVTHRQLSEVYIKWQKHSQLLKDSDFSQ  
 EPIMALRTVILEILMEKEMDNSQRECIKDILTKHLVELSILARTFKNTQLPERAIFQIKQYNS  
 VSCGVSEWQLEEAQVFWAKKEQSLALSILKQMIKKLDASCAANNPSLKLTYTECLRVC  
 NWLAETCLENPAVIMQTYLEKAVEVAGNYDGESSDELNRNGKMKAFSLARFSDTQYQR  
 IENYMKSSEFENKQALLKRAKEEVGLLREHKIQTNRYTVKVQRELELDELALRALKEDRK  
 RFLCKAVENYINCLLSGEEHDMWVFRCLSLWLENSGVSEVNGMMKRDGMKIPTYKFLP  
 LMYQLAARMGTMKGGLGFHEVLNNLISRISMDHPHHTLFIILALANANRDEFLTKEVA  
 RRSRITKNVPKQSSQLDEDRTAANRIICTIRSRRPQMVRSEALCDAYIILANLDATQW  
 KTQRKGINIPADQPITKLKNLEDVVVPTMEIKVDHTGEYGNLVTIQSFKAEFRLAGGVNLP  
 KIIDCVGSDGKERRQLVKGRDDLQDAVMQQVFQMCNTLLQRNTETRKRKLTICTYKV  
 VPLSQRSGVLEWCTGTVPIGEFLVNNEDGAHKRYRPNDFAFQCQKKMMEVQKKSFE  
 EKYEVFMDVCQNFQPVFRYFCMEKFLDPAIWFEKRLAYTRSVATSSIVGYILGLGDRHV  
 QNILINEQSAELVHIDLGVAFEQGKILPTPETVPFRLTRDIVDGMGITGVEGVFRRCCCKT  
 MEVMRNSQETLLTIVEVLLYDPLFDWTMNPLKALYLQQRPEDETELHPTLNADDQECK

RNLSDIDQSFDKVAERVLMRLQEKLKGVEEGTVLSVGGQVNLLIQQAIDPKNLSRLFPG  
WKAWV

SEQID No:104

MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLYMVVGTLA  
AIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSDINDTGFFMNLEEDMTRYAYY  
YSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQFFHAIMRQEIGWFDVHDVGELNTRLTD  
DVSKINEGIGDKIGMFFQSMATFFTGFIVGFTRGWKLT LVILAISPVLGLSAAVWAKILSSF  
TDKELLAYAKAGAVAEVLAARTVIAFGGQKKELERYNKNLEEAKRIGIKKAITANISIGA  
AFLLIYASYALAFWYGTTLVLSGEYSIGQVLT VFFSVLIGAFSVGQASPSIEAFANARGAA  
YEIFKIIDNKPSIDSYSGHKKPDNIKGNLEFRNVHFSYPSRKEVKILKGLNLKVQSGQTV  
ALVGNSGCGKSTTVQLMQRLYDPTEGMVSVDGQDIRTINVRFLREIIGVVSQEPVLFAT  
TIAENIRYGRENVMTDEIEKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAIA  
RALVRNPKILLDEATSALDTESEAVVQVALDKARKGRTTIVIAHRLSTVRNADVIAGFDD  
GVIVEKGNHDELMKEKGIYFKLVTMQTAGNEVELENAADESKSEIDALEMSSNDSRSSLI  
RKRSTRRSVRGSQAQDRKLSTKEALDESIPPVSFWRIMKLNLTWPYFVVGVFCAIING  
GLQPAFAIIFSKIIGVFTRIDDPETKRQNSNLF SLLFLALGIISFITFFLQGFTFGKAGEILTK  
RLRYMVFRSMLRQDVSWFDDPKNTTGALTTRLANDAAQVKGAIGSRLAVITQNIANLGT  
GIIISFIYGWQLTLLLLAIVPIIAIAGVVEMKMLSGQALKDKKELEGAGKIAIEINFRTVVS  
LTQEQKFEHMYAQSLQVPYRNSLRKAHIFGITFSFTQAMMYFSYAGCFRFGAYLV AHKL  
MSFEDVLLVFSVAVFGAMAVGQVSSFAPDYAKAKISAHHIIMIEKTPLIDSYSTEGLMPN  
TLEGNVTFGEVVFNYPTRPDIPVLQGLSLEVKKGQTLALVGSSGCGKSTVVQLLERFYD  
PLAGKVLLDGKEIKRLNVQWLRAHLGIVSQEPILFDCSIAENIAYGDNSRVVSQEEIVRAA  
KEANIHAFIESLPNKYSTKVGDKGTQLSGGQKQRIAARALVRQPHILLDEATSALDTES  
EKVVQEALDKAREGRTCIVIAHRLSTIQNADLIVVFQNGRVKEHGTHQQLLAQKGIYFSM  
VSVQAGTKRQ

SEQID No:105

MFSLSSTVQPQFTVPLSHLINAFTPKNTSVSLSGVSVSQNQHRDVVPEHEAPSSECM  
FSDFLTCLNIVSIGKGKIFEGYRSMFM EPAKRMKKSLDTTDNWHIRPEPFSLSIPPSLNL  
DLGLSELKIGQIDQLVENLLPGFCKGKNISHWHTSHVSAQSFFENKYGNLDIFSTLRSS  
CLYRHHSRALQSICSDLQYWPVFIQSRGFKTLKSRTTRRLQSTSERLAETQNIAPSFVKG  
FLLRDRGSDVESLDKLMKTKNIPEAHQDAFKTGFAEGFLKAQALTQKTNDLSLRRTRLILF  
VLLLFGIYGLLKNPFLSVRFRTTTGLDSAVDPVQMKNVTFEHVKGVEEAKQELQEVEF

LKNPQKFTILGGKLPKGILLVGPPGTGKTLLARAVAGEADVPFYYASGSEFDEMFGVGVG  
 ASRIRNLFREAKANAPCVIFIDE LDSVGGKRIESPMHPYSRQTINQLLAEMDGFKNPNEG  
 IIGATNFPEALDNALIRPGRFDMQVTVPRPDVKGRTEILKWYLNKIKFDQSVDP EIIARGT  
 VGFSGAELENLVNQAALKA AVDGKEMVTMKELEFSKDKILMGPERRSVEIDNKNKTITA  
 YHESGHAIAYYTKDAMPINKATIMPRGPTLGHV SLLPENDRWNETRAQLLAQMDVSMG  
 GRVAEELIFGTDHITTGASSDFDNATKIAKRMVTKFGMSEKLGVM TYSDTGKLSPETQS  
 AIEQEIRILLRDSYERAKHILKTHAKEHKNLAEALLTYETLDAKEIQIVLEGKKLEVR

SEQID No:106

MDPSMGVNSVTISVEGMTCN SCVWTIEQQIGKVNGVHHIKVSLEEKNATIIYDPKLQTPK  
 TLQEAIDDMGFD AVIHNPDPVLTDTLFLT V TASLTLPWDHIQSTLLKTKGVTDIKIYPQK  
 RTVAVTIIPSIVNANQIKELVPELSLDTGTLEKKSGACEDHSMAQAGEVVLKMKVEGMTC  
 HSCTSTIEGKIGKLQGVQRIKVSLDNQEATIVYQPHLISVEEMKKQIEAMGFPAFVKKQP  
 KYLKLGAIDVERLKNTPVKSSSEGSQQRSPSYTNDSTATFIIDGMHCKSCVSNIESTLSAL  
 QYVSSIVVSLENRSAIVKYNASSVTPESLRKAIEAVSPGLYRV SITSEVESTSNSPSSSSL  
 QKIPLNVVSQPLTQETVINIDGMTCN SCVQSIEGVISKKPGVK SIRVSLANSNGTVEYDPL  
 LTSPETLRGAIEDMGFDATLSDTNEPLV VIAQPSSEMPLLTSTNEFYTKGMTPVQDKEE  
 GKNSSKCYIQVTGMTCASCVANIERNLRREEGIYSILVALMAGKAEVRYNPAVIQPPMIA  
 EFIRELGFGATVIENADEGDGVLELVVRGMTCASCVH KIESSLTKHRGILYCSVALATNK  
 AHIKYDPEIIGPRDIIHTIESLGFEASLVKKDRSASHLDHKREIRQWRRSFLVSLFFCIPVM  
 GLMTYMMVMDH H FATHHNQNMSKEEMINLHSSMF LERQILPGLSVMNLLSFLLCVPV  
 QFFGGWYFYIQAYKALKHKTANMDVLIVLATTIAFAYS LIILLVAMYERAKVNPITFFDTPP  
 MLFVFIALGRWLEHIAKGKTSEALAKLISLQATEATIVTLDS DNILLSEEQVDVELVQRGDII  
 KVVPGGKFPVDGRVIEGHSMVDESLITGEAMPVAKKPGSTVIAGSINQNGSLLICATHVG  
 ADTTLSQIVKLVEEAQTSKAPIQQFADKLSGYFVPFIVFVSIATLLVWIVIGFLNFEIVETYF  
 PGYNRSISRTE TIIRFAFQASITVLCIACPCSLGLATPTAVMVG TGVGGAQNGILIKGGEPL  
 MAHKVKVVVFDKTGTITHGTPVVNQVKVLTESNRISHHKILAIVGTAESNSEHPLGTAITK  
 YCKQELDTETLGT CIDFQVVP GCGISCKVTNIEGLLHKNNWNIEDNNIKNASLVQIDASN  
 EQSSTSSSMIIDAQISNALNAQQHKVLIGNREWMIRNGLVINNDVNDFMTEHERKGR TA  
 VLVAVDDEL CGLIAIADTVKPEAE LAIHILKSMGLEVV LMTGDNSKTARSIASQVGITKVFA  
 EVLP SHKVAKV KQLQEEGKRVAMVG DGINDSPALAMANVGIAIGTGTDVAIEAADVVLIR  
 NDLLDVVASIDLSRKT VKRIRINFVFALIYNLVGIPIAAGVFMP IGLVLQPWMGSAAMAAS  
 SVSVVLSSLFLKLYRKPTYESYELPARSQIGQKSPSEISVHV GIDDTSRNSPKLGLLDRIV  
 NYSRASINSLLSDKRSLNSVVTSEPDKHSLLVGDFREDDDTAL



SEQID No:107

METPAAAAPAGSLFPSFLLLACGTLVAALLGAAHRLGLFYQLLHKVDKASVRHGGENVA  
 AVLRAHGVRFIFTLVGGHISPLLVACEKLGIRVVDTRHEVTAVFAADAMARLSGTVGVAA  
 VTAGPGLTNTVTAVKNAQMAQSPILLGGAASTLLQNRGALQAVDQLSLFRPLCKFCVS  
 VRRVRDIVPTLRAAMAAAQSGTPGPVFVELPVDVLYPYFMVQKEMVPAKPPKGLVGRV  
 VSWYLENYLANLFAGAWEPQPEGPLPLDIPQASPPQVQRCVEILSRAKRPLMVLSQA  
 LLTPTSADKLRAAVETLGVPCLGGMARGLLGRNHPLHIRENRSAAKKADVIVLAGTVC.  
 DFRLSYGRVLSHSSKIIIVNRNREEMLLNSDIFWKPQEAVQGDVGSFVLKLVEGLQGGQT  
 WAPDWVEELREADRQKEQTFREKAAMPVAQHLNPVQVLQLVEETLPDNSILVVDGGD  
 FVGTAHLVQPRGPLRWLDPGAFGTLGVGAGFALGAKLCRPDAEVWCLFGDGAFGYS  
 LIEFDTFVRHKIPVMALVGNDAGWTQISREQVPSLGSNVACGLAYTDYHKAAMGLGAR  
 GLLSRENEQVVKVLHDAQQQCRDGHPVVVNILIGRTDFRDGSIIV

SEQID No:108

MPVLSRPRPWGNTLKRRTAVLLALAAAYGAHKVYPLVRQCLAPARGLQAPAGEPTQEAS  
 GVAAAKAGMNRVFLQRLLWLLRLLFPRVLCRETGLLALHSAALVSRTFLSVYVARLDGR  
 LARCIARKDPRAFGWQLLQWLLIALPATFVNSAIRYLEGQLALSFRSRLVAHAYRLYFSQ  
 QTYRVSNDGRLRNPQSLTEDVVAFAASVAHLYSNLTKPLLDVAVTSYTLLRAARSR  
 GAGTAWPSAIALGLVVFLTANVLRAFSPKFGELVAEEARRKGELRYMHSRVVANSEEIAF  
 YGGHEVELALLQRSYQDLASQINLILLERLWYVMLEQFLMKYVWSASGLLMVAVPIITAT  
 GYSESDAEAVKKALEKKEEELVSETEAFTIARNLLTAAADAIERIMSSYKEVTELAGYT  
 ARVHEMFQVFEDVQRCHFKRPRELEDAQAGSGTIGRSGVRVEGPKIRGQVVDVEQGI  
 ICENIPIVTPSGEVVVASLNIRVEEGMHLLITGPNGCGKSSLFRILGGLWPTYGGVLYKPP  
 PQRMFYIPQRPYMSVGSRLDQVIYPDSVEDMQRKGYSEQDLEAILDVVHLHHILQREG  
 GWEAMCDWKDVLSGGGEKQRIGMARMFYHRPKYALLDECTSAVSIDVEGKIFQAAKDA  
 GIALLSITHRPSLWKYHTHLLQFDGEGGWKFELDSAARLSLTEEKQRLEQQLAGIPKM  
 QRRLQELCQILGEAVAPAHVPAPSPQGPGGLQGAST

SEQID No:109

MGAAVFFGCTFVAFGPALFLITVAGDPLRVILVAGAFFWLVSLLLASVWVILVHVTD  
 RSDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVS  
 GLSFGIISGVFSVINILADALGPGVVGIIHGDSPIYFLTSAFLTAAIILLHTFWGVVFFDACE



RRRYWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRS  
LLCRRQEDSRVMVYSALRIPPED

SEQID No:110

MYEGKKTKNMFLTRALEKILADKEVKKAHHSQLRKACEVALEEIKAETEKQSPPHGEAK  
AGSSTLPPVKSKTNFIEADKYFLPFELACQSKCPRIVSTSLDCLOKLIAYGHILTGNAPDST  
TPGKKLIDRIIETICGCFQGPQTDEGVQLQIIKALLTAVTSQHIEIHEGTVLQAVRTCYNIL  
ASKNLINQTTAKATLTQMLNVIFARMENQALQEAKQMEKERHRQHHLHPSPVSHHEP  
ESPQLRYLPPQTVDHISQEHEGDLHTNDVDKSLQDDTEPENGSDISSAENEQTEAD  
QATAAETLSKNEVLYDGENHDCEEKPDIVQNIVEEMVNIVVGDMGEGTTINASADGNI  
GTIEDGSDSENIQANGIPGTPISVAYTPSLPDDRLSVSSNDTQESGNSSGPSPGAKFSHI  
LQKDAFLVFRSLCKLSMKPLSDGPPDPKSHELRSKILSLQLLSILQNAGPIFRTNEMFIN  
AIKQYLCVALSKNGVSSVPEVFELSLSIFLTLLSNFKTHLKMQUIEVFFKEIFLYILETSTSSF  
DHKWMVIQTLTRICADAQSVVDIYVNYDCDLNAANIFERLVNDLSKIAQGRGSQELGMS  
NVQELSLRKKGLECLVSISKCMVEWSKDQYVNPNSQTTLGQEKPEQEMSEIKHPETIN  
RYGSLNSLESTSSSGIGSYSTQMSGTDNPEQFEVLKQQKEIIEQGIDLFNKKPKRGIQYL  
QEQGMLGTTPEIDIAQFLHQEERLDSTQVGEFLGDNDKFNKEVMYAYVDQHDFSGKDF  
VSALRMFLEGFRLPGEAQKIDRLMEKFAARYLECNQGQTLFASADTAYVLAYSIIMLTTD  
LHSPQVKNKMTKEQYIKMNRGINDSKDLPEEYLSAIYNEIAGKKISMKETKELTIPTKSSK  
QNVASEKQRRLLYNLEMEQMAKTAKALMEAVSHVQAPFTSATHLEHVRPMPFKLAWTP  
FLAAFSVGLQDCDDTEVASLCLEGIRCAIRIACIFSILQERDAYVQALARFTLLTVSSGITE  
MKQKNIDTIKTLITVAHTDGNLYLGNWHEILKCISQLKLAQLIGTGKPRYISGTVRGREG  
SLTGTKDQAPDEFVGLGLVGGNVWDWKQIASIQESIGETSSQSVVAVDRIFTGSTRLDG  
NAIVDFVRWLCAVSMDELLSTTHPRMFSLQKIVEISYYNMGRIRLQWSRIWEVIGDHFNK  
VGCNPNEEDVAIFAVDSLRLQSLMKFLEKGELANFRFQKDFLRPFHEHIMKRNRSPRTIRDMV  
VRCIAQMVNSQAANIRSGWKNIFS VFHLAASDQDESIVELAFQTTGHIVTLVFEKHFPATI  
DSFQDAVKCLSEFACNAAFPDTSM EAIRLIRHCAKYVSDRPQAFKEYTSDDMNVPED  
RVWVRGWFPILFELSCIINRCKLDVRTRGLTVMFEIMKTYGHTYEKHHWWQDLFRIVFRIF  
DNMKLPEQQTEKA EWMTTTCNHALYAICDVFTQYLEVLSDVLLDDIFAQLYWCVQQDN  
EQLARSGTNCLENVVILNGEKFTLEIWDKTCNCTLDIFKTTIPHALLTWRPNSETAPP  
PSPVSEKPLDTISQKSVDIHDSIQPRSDNRPAPLVSASAVNEEVSKI KSTAKFPEQKL  
FAALLIKCVVQLELIQTIDNIVFFPATSKKEDAENLAAAQRDAVDFDVRVDTQDQGM YRF  
LTSQQLFKLLDCLLESHRFAKAFNSNNEQRTALWKAGFKGKSKPNLLKQETSSLACGLR

ILFRMYMDES RVSAWEEVQQRLLNVCSEALSYFLT LTSESHREAWTNLLLLFLT KVLKIS  
DNRFKAHASFYYPLLCEIMQFDLIPELRAVLRRFFLRIGVVFQISQPPEQE LGINKQ

SEQID No:111

MAVSRLDRLFILLDTGTTPVTRKAAAQQLGEVVKLHPHELNNLLSKVLIYLR SANWDTRI  
AAGQAVEAIVKNVPEWNPVPRTRQEPTSESSMEDSPTTERLNFD RFDICRLLQH GASLL  
GSAGAEFEVQDEKSGEVDPKERARQRKLLQKKLGLNMGEAIGMSTEELFNDEDLDYT  
PTSASFVNKQPTLQAAELIDSEFRAGMSNRQKNKAKRMAKLF AKQRSRDAVETNEKSN  
DSTDGEPEEKRRKIANVVINQSANDSKVLIDNIPDSSSLIETNEWPLESFCEELCNDLFN  
PSWEVRHGAGTGLREILKAHGKSGGKMGDSTLEEMIQQH QEWLEDLVIRLLCVFALDR  
FGDFVSDEVVAPVRETCAQTLGVVLKHMNETGVHKTVDVLLKLLTQEQWEVRHGGLLG  
IKYALAVRQDVINTLLPKVLTRII EQLQDLDDVRAVAAASLVPVVESLVYLQTQKVPFIIN  
TLWDALLELDDLTASTNSIMTLLSSLLTYPQVQQCSIQQSLTVLVPRVWPFLHHTISSVR  
RAALETFLTLLSTQDQNSSSWLIPILPDMLRHIFQFCVLESSQEILDLIHKVWMELLSKAS  
VQYVVAAACPWMGAWLCLMMQPSHLPIDLNMLLEV KARAKEKTGGKVRQGGQSQNKE  
VLQEYIAGADTIMEDPATRDFVVMRARMMAAKLLGALCCCICDPGVNVVTQEIKPAESL  
GQLLLFHLNSKSALQRISVALVICEWAALQKECKAVTLAVQPRLLDILSEHLYYDEIAVPF  
TRMQNECKQLISSLADVHIEVGNRVNNNVLTIDQASDLVTTVFNEATSSFDLNPQVLQQ  
LDSKRQQVQMTVTETNQEWQVLQLRVHTFAACAVVSLQQQLPEKLNPIIKPLMETIKKEE  
NTLVQNYAAQCIAKLLQQCTTRTPCPNSKIIKNLCSSLCVDPYLTPCVTCPVPTQSGQEN  
SKGSTSEKDGMHHTVTKHRGIITLYRHQKA AFAITSRRGPTPKAVKAQIADLPAGSSGNI  
LVELDEAQKPYL VQRRGAEFALT TIVKHFGGEMAVKLPHLWDAMVGPLRNTIDINNFDG  
KSLLDKGDSPAQELVNSLQVFETA AASMDSELHPLL VQHLP HLYMCLQYPSTAVRHMA  
ARCVGVMSKIATMETMNIFLEKVLPWLGAIDDSVKQEGAIEALACVMEQLDVGIVPYIVLL  
VVPVLGRMSDQTD SVRFMATQCFATLIRLMPLEAGIPDP PNMSAELIQLKAKERHFLEQ  
LLDGKKLENYKIPVPINAELRKYQQDGVNWL AFLN KYKLHGILCDDMGLGKTLQSICILA  
GDHCHRAQEYARSKLAECMPLPSLVVCPPTLTGHWVDEVGKFCSREYLNPLHYTGPP  
TERIRLQH QVKRHN LIVASYDVVRNDIDFFRNIKFNYCILDEGHV IKN GKTKLSKAVKQLT  
ANYRIILSGTPIQNNVLELWSLFD FLMPGFLGTERQFAARYGKPILASRDARSSSREQEA  
GVLAMDALHRQVLPFLLRMKEDVLQDLPPKIIQDYYCTLSPLQVQLYEDFAKSRAKCD  
VDET VSSATLSEETEKPKLKATGHVFQALQYLRKLCNHPALVLT PQHPEFKTTAEKLAV  
QNSSLHDIQHAPKLSALKQLLLDCGLGNGSTSESGTESVVAQHRILIFCQLKSMLDIVEH  
DLLKPHLPSVTYLRLDGSIPPGQRHSIVSRFNNDPSIDVLLL TTHVGGGLGLNLTGADTVV  
FVEHDWNPMRDLQAMDRAHRIGQKR VNVYRLITRG TLEEKIMGLQKFKMNIANTVISQ

ENSSLQSMGTDQLLDLFTLDKDGKAEKADTSTSGKASMKSILENLSDLWDQEQYDSEY  
SLENFMHSLK

SEQID No:112

MGGRVFLAFCVWLTLPGAETQDSRGCARWCPQNSSCVNATACRCNPGFSSFSEIITTP  
TETCDDINECATPSKVSCGKFSDCWNTEGSYDCVCSPGYEPVSGAKTFKNESENTCQ  
DVDECQQNPRLCKSYGTCVNTLGSYTCQCLPGFKFIPEDPKVCTDVNECTSGQNPCH  
SSTHCLNNVGSYQCRCPGWQPIPGSPNGPNNTVCEDVDECSSGQHQCDSSTVCFN  
TVGSYSCRCRPGWKPRHGIPNNQKDTVCEDMTFSTWTPPPGVHSQTLRFFDKVQDL  
GRDSKTSSAEVTIQNVIKLVDELMEAPGDVEALAPPVRHLIATQLLSNLEDIMRILAKSLP  
KGPFTYISPSNTELTLMIQERGDKNVTMGQSSARMKLNWAVAAGAEDPGPAVAGILSIQ  
NMTTLLANASLNLHSHKKQAELEEIYESSIRGVQLRRLSAVNSIFLSHNNTKELNSPILFAF  
SHLESSDGEAGRDPAPAKDVMPGPRQELLCAFWKSDSDRGGHWATEVCQVLGSKNGS  
TTCQCSSLSSFTILMAHYDVEDWKLTLITRVGLALSFLCILLCILTFLLRPIQGSRTTIHL  
HLCICLFGVSTIFLAGIENEGGQVGLRCRLVAGLLHYCFLAFCWMSLEGLELYFLVVRV  
FQQQGLSTRWLCLIGYGVPLLIVGVSAAIYSKGYGRPRYCWLDFEQGFLWSFLGPVTFII  
LCNAVIFVTTWKLTKKFSEINPDMKKLKKARALTITAIQFLLGCTWVFGLFIFDDRSLV  
LTYVFTILNCLQGAFLYLLHCLLNKKVREEYRKWACL VAGGSKYSEFTSTTSGTGHNQT  
RALRASESGI

SEQID No:113

SLQWTAVATFLYAEVFVLLLCIPFISPKRWQKIFKSRLVELLVSYGNTFFVVLIVILVLLVI  
DAVREIRKYDDVTEKVNLONNPGAMEHFHMKLFRAQRNLYIAGFSLLLSFLLRRLVTLIS  
QQATLLASNEAFKKQAESASEAAKKYMEENDQLKKGAAVDGGKLDVGNAEVLKEEEN  
RSLKADLQKLKDELASTKQKLEKAENQVLAMRKQSEGLTKEYDRLLLEEHAQLQAAVDG  
PMDKKEE

SEQID No:114

MSFLIDSSIMITSQILFFGFGWLFFMRQLFKDYEIRQYVVQVIFSVTFASFCTMFELIIFEIL  
GVLNSSSRYFHWKMNL CVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTFMYFF  
WKLGDPPILSPKHGILSIEQLISRVGVIGVTLMALLSGFGAVNCPYTYMSYFLRNVTDTD  
ILALERRLLQTMDMIISKKKRMAMARRTMFQKGEVHNKPSGFWGMIKSVTTSASGSEN  
TLIQQEVDALEELSRQLFLETADLYATKERIEYSKTFKGKYFNFLGYFFSIYCVWKIFMATI  
NIVFDRVGKTDVPVTRGIEITVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLITLTKFFYAIS

SSKSSNVIVLLLAQIMGMVFVSSVLLIRMSMPLEYRTIITEVLGELQFNFYHRWFDVIFLVS  
ALSSILFLYLAHKQAPEKQMAP

SEQID No:115

GEGGESWPPPVFRVRGFGVVALTCSSATADPPSALSSRRSVPPGQLCEAAAGEGTMG  
TVHARSLEPLPSSGPDFGGLGEEAEFVEVEPEAKQEILENKDVVVQHVHFDGLGRTKD  
DIIICEIGDVFKAKNLIEMRKSHEAREKLLRLGIFRQVDVLIDTCQGDDALPNGLDVTFEV  
TELRRLTGSYNTMVGNNEGSMVLGLKLPNLLGRAEKVTFQFSYGTKETSYGLSFFKPR  
PGNFERNFSVNLYKVTGQFPWSSLRETDRGMSAEYSFPIWKTSHTVKWEGVWRELGC  
LSRTASFAVRKESGHSLKSSLSHAMVIDSRNSSILPRRGALLKVNQELAGYTGGDVFSIK  
EDFELQLNKQLIFDSVFSASFWGGMLVPIGDKPSSIADRFYLGGPTSIRGFSMHSIGPQS  
EGDYLGGGEAYWAGGLHLYTLPFRPGQGGFGELFRTHFFLNAGNLCNLNYGEGPKAHI  
RKLAECIRWSYGAGIVLRLGNIARLELNYCVPMGVQTGDRICDGVQFGAGIRFL

SEQID No:116

MALAVSLPLALSPPRLLLLLLSLLPVARASEAEHRLFERLFEDYNEIIRPVANVSDPVIIHF  
EVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKPDIV  
LYNNAVGDFQVDDKTKALLKYTGEVTWIPPAIFKSSCKIDVTYFPFDYQNCTMKFGSWS  
YDKAKIDLVLIGSSMNLKDYWESGEWAIKAPGYKHDIKYNCCIEIYPDITYSLYIRRLPLF  
YTINLIIPCLLISFLTVLVFLPSDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVIPLIGEYLLF  
TMIFVTLSIVITVFVLNVHYRTPTTHTMPSWVKTVFLNLLPRVMFMTRPTSNEGNAQKPR  
PLYGAELSNLNCFSRAESKGCKEGYPCQDGMCGYCHHRIKISNFSANLTRSSSESSESV  
DAVLSLSALSPEIKEAIQSVKYIAENMKAQNEAKEIQDDWKYVAMVIDRIFLWVFTLVCIL  
GTAGLFLQPLMAREDA

SEQID No:117

MGSRASTLLRDEELEEIKKETGFSSHSQITRLYSRFTSLDKGENGTLSREDFQRIPELAINP  
LGDRIINAFPEGEDQVNFRGFMRTLAHFRPIEDNEKSKDVNGPEPLNSRSNKLHFAFR  
LYDLKDEKISRDELLQVLRMMVGVNISDEQLGSIADRTIQEADQDGD SAISFTEFVKVL  
EKVDVEQKMSIRFLH

SEQID No:118

MASESSPLLAYRLLGEEGVALPANGAGGPGGASARKLSTFLGVVVPTVLSMFSIVVFLRI  
GFVVGHAGLLQALAMLLVAYFILALTVLSVCAIATNGAVQGGGAYFMISRTLGPVGGSI



GLMFYLANVCGCAVSLLGLVESVLDVFGADATGPSGLRVLPQGYGWNLLYGSLLLGLV  
 GGVCTLGAGLYARASFLTFLLVSGSLASVLISFVAVGPRDIRLTTPRPGPNGSSLPPRFGH  
 FTGFNSSTLKDNLGAGYAEDYTTGAVMNFANVFAVLFFNGCTGIMAGANMSGELKDPSR  
 AIPLGTIVAVAYTFFVYVLLFFLSSFTCDRTLLQEDYGFFRAISLWPPLVLIGIYATALSAS  
 MSSLIGASRILHALARDDLFGVILAPAKVVSRRGNPWAAVLYSWGLVQLVLLAGKLNTLA  
 AVTVFYLVAYAAMDLSCLSLEWASAPNFRPTFSLFSWHTCLLGVASCLLMMFLISPGA  
 AGGSLLLMGLLAALLTARGGPSSWGYVSQALLFHQVRKYLLRLDVRKDHVKFWRPQLL  
 LLVGNPRGALPLLRLANQLKKGGLYVLGHVTLGDLDLSPSDPVQPQYGAWLSLVDRAQ  
 VKAFVDLTFSPSVRQGAQHLLRISGLGGMKPNTLVLGfyDDAPPQDHFLTDPAFSEPAD  
 STREGSSPALSTLFPPPRAPGSPRALNPQDYVATVADALKMNKNVVLARASGALPPER  
 LSRGSGGTSQ LHHVDVWPLNLLRPRGGPGYVDVCGLFLLQMATILGMVPAWHSARLRI  
 FLCLGPREAPGAAEGRLRALLSQLRIRAEVQEVVWGEGAGAGEPEAEEEGDFVNSGR  
 GDAEAEALARSANALVRAQQGRGTGGGPGGPEGGDAEGPITALTFLYLPRPPADPAR  
 YPRYLALLETLTRDLGPTLLVHGVTPVTCTDL

SEQID No:119

MASFVTEVLAHSGRLEKEDLGTRISRLTRRVEEIKGEVCNMISKKYSEFLPSMQSAQGLI  
 TQVDKLSEDIDLLKSRIESEVRRDLHVSTGEFTDLKQQLERDSVVL SLLKQLQEFSTAIEE  
 YNCALTEKKYVTGAQRLEEAQKCLKLLKSRKCFDLKILKSLSMELTIQKQNILYHLGEEW  
 QKLIVWKFPFSKDTSSLESYLQTELHLYTEQSHKEEKTMPPISSVLLAFSVLGELHSL  
 KSFGQMLLKYILRPLASCP SLHAVIESQPNIVIIRFESIMTNLEYPSPSEVFTKIRLVLEV LQ  
 KQLLDLPLD TDLENEKTSTVPLAEM LGDMIWEDLSECLIKNCLVYSIPTNSSKLQQYEEII  
 QSTEEFENALKEMRFLKGD TTDLLKYARNINSHFANKKCQDVIVAARNLMTSEIHNTVKII  
 PDSKINVPELPTPDEDNKLEVQKVSNTQYHEVMNLEPENTLDQHSFSLPTCRISES VKK  
 LMELAYQTLLEATTSSDQCAVQLFYSVRNIFHLFHDVVPTYHKENLQKLPQLAAIHHNNC  
 MYIAHHLLTLGHQFRLRLAPILCDGTATFVDLVPGFRRLGTECF LAQMRAQKGELLERLS  
 SARNFSNMDD EENYSAASKAVRQVLHQLKRLGIVWQDVLPVNIYCKAMGTLLNTAISEV  
 IGKITALEDISTEDGDRLYSLCKTVMDEGPQVFAPLSEESKNKKYQEEVPVYVPKWMPF  
 KELMMMLQASLQEIGDRWADGKGPLAAAFSSSEVKALIRALFQNTERRAAALAKIK

SEQID No:120

MSRLGALGGARAGLGLLLGTAAGLGFLCLLYSQRWKRTQRHGRSQSLPNSLDYTQTS  
 DPGRHVMLLRAVPGGAGDASVLP SLPREGQEKVLDRLDFVLTS LVALRREVEELRSSL  
 RGLAGEIVGEVRCHMEENQRVARRRRRFPFVRERSDSTGSSSVYFTASSGATFTDAESE

GGYTTANAESDNERDSDKESEDEGEDEVSCETVKMGRKDSLDEEEAASGASSALEAG  
 GSSGLEDVLPLLQQADELHRGDEQGKREGFQLLLNNKLVYGSRQDFLWRLARAYSDM  
 CELTEEVSEKKSYALDGKEEAEEALEKGDESADCHLWYAVLCGQLAEHESIQRRIQSGF  
 SFKEHVDKAIALQPENPMAHFLLGRWCYQVSHLSWLEKKTATALLESPLSATVEDALQS  
 FLKAEELQPGFSKAGRVIYISKCYRELGKNSEARWWWMLALELPDVTKEDLAIQKDLEEL  
 EVILRD

SEQID No:121

EIEQNSAMAPRKRGGRGISFIFCCFRNNDHPEITYRLRNDNSNFALQTMEPALPMPPVEE  
 LDVMFSELVDELDTDKHREAMFALPAEKKWQIYCSKKKDQEEENKGATSWPEFYIDQL  
 NSMAARKSLLALEKEEEEEERSKTIESLKTALRTKPMRFVTRFIDLDGLSCILNFLKTMDYE  
 TSESRIHTSLIGCIKALMNNSQGRAHVLAHSESINVIAQSLSTENIKTKVAVLEILGAVCLV  
 PGGHKKVLQAMLHYQKYASERTRFQTLINDLDKSTGRYRDEVSLKTAIMSFINAVLSQG  
 AGVESLDFRLHLRYEFLMLGIQPVIDKLREHENSTLDRHLDFFEMLRNEDELEFAKRFEL  
 VHIDTKSATQMFELTRKRLTHSEAYPHFMSILHHCLQMPYKRSGNTVQYWLLLDRIIQQI  
 VIQNDKGQDPDSTPLENFNIKNVVRMLVNENEVKQWKEQAEMRKEHNELQQKLEKK  
 ERECDAKTQEKEEMMQTLNKMKEKLEKETTEHKQVKQQVADLTAQLHELSSRAVCASI  
 PGGPSPGAPGGPFPSSVPGSLLPPPPPPPLPGGMLPPPPPPPLPPGGPPPPPPGPPPLG  
 AIMPPPGAPMGLALKKKSIPQPTNALKSFNWSKLPENKLEGTWTEIDDTKVFKILDLED  
 LERTFSAYQRQQDFFVNSNSKQKEADAIDDTLSSKLKVKELSVIDGRRRAQNCNILLSRLK  
 LSND EIKRAILTMDEQEDLPKDMLEQLLK FVPEKSDIDLLEEHKHELDRMAKADRFLFEM  
 SRINHYQQRLQSLYFKKKFAERVAEVKPKVEAIRSGSEEVFRSGALKQLLEVVLAFGN  
 MNKGQRGNAYGFKISSLNKIADTKSSIDKNITLLHYLITIVENKYPSVLNLNEELRDIPQAA  
 KVNMTELDKEISTLRSGLKAVETELEYQKSQPPQPGDKFVSVVSQFITVASFSFSDVEDL  
 LAEAKDLFTKAVKHFGEEAGKIQPDEFFGIFDQFLQAVSEAKQENENMRKKKEEEEERRA  
 RMEAQLKEQRERERKMRKAKENSEESGEFDDLVSALRSGEVFDKDLSKLKRNRKRITN  
 QMTDSSRERPITKLN

SEQID No:122

MTVFRQENVDDYYDTGEELGSGQFAVVKKCREKSTGLQYAAKFIKKRRTKSSRRGVSR  
 EDIEREVSILKEIQHPNVITLHEVYENKTDVILILELVAGGELFDFLAEKESLTEEEATEFLK  
 QILNGVYYLHSLQIAHFDLKPENIMLLDRNVPKPRIKIIDFGLAHKIDFGNEFKNIFGTPEFV  
 APEIVNYEPLGLEADMWSIGVITYILLSGASPFLGDTKQETLANVSAVNYESFEDEYFSNT  
 SALAKDFIRRLLVKDPKKRMTIQDSLQHPWIKPKDTQQALS RKASAVNMEKFKKFAARK

KWKQSVRLISLCQRLSRSFLSRSNMSVARSDDTLDEEDSFVMKAIHAINDDNVPGLQH  
 LLGSLSNYDVNQPNKHGTPPLLIAAGCGNIQILQLLIKRGSRIDVQDKGGSNAVYWAARH  
 GHVDTLKFLSENKCPLDVKDKSGEMALHVAARYGHADVAQVTCAASAQIPISRTKEEET  
 PLHCAAWHGYYSVAKALCEAGCNVNIKNREGETPLLTASARGYHDIVECLAHEHGADLN  
 ACDKDGHIHLAVRRRCQMEVIKTLLSQGCFVDYQDRHGNTPLHVACKDGNMPIVVAL  
 CEANCNLDISNKYGRTPHLAANNGILDVVRYLCLMGASVEALTTDGKTAEDLARSEQH  
 EHVAGLLARLRKDTHRGLFIQQLRPTQNLQPRIKLKLFHSGSGKTTLVESLKCGLLRSF  
 FRRRRPRLSSTNSSRFPPSPLASKPTVSVSINNLYPGCENVSVRSRSMMFEPGLTKGM  
 LEVFAVAPTHHPHCSADDQSTKAIDIQNAYLNGVGDFSWEFSGNPVYFCCYDYFAAND  
 PTSIHVVVFSLEEPYEIQLNPVIFWLSFLKSLVPVEEPIAFGGKLKNPLQVVLVATHADIMN  
 VPRPAGGEFGYDKDTSLLKEIRNRFGNDLHISNKLFLVDAGASGSKDMKVLNRNHLQEIR  
 SQIVSVCPPMTHLCEKIISTLPSWRKLNGPNQLMSLQQFVYDVQDQLNPLASEEDLRRI  
 AQQHSTGEINIMQSETVQDVLLLDPRWLCTNVLGKLLSVETPRALHHYRGRYTVEDIQ  
 RLVPDSDVEELLQILDAMDICARDLSSGTMVDVPALIKTDNLHRSWADEEDEVMVYGGV  
 RIVPVEHLTPFPCGIFHKVQVNLCRWIHQQSTEGDADIRLWVNGCKLANRGAELLVLLV  
 NHGQGIEVQVRGLETEKIKCCLLLDSVCSTIENVMATTLPGLLTVKHLYSPQQQLEHHEP  
 VMIYQPRDFFRAQTLKETSLTNTMGGYKESFSSIMCFGCHDVYSQASLGMDIHASDLNL  
 LTRRKLSRLLDPPDPLGKDWCLLAMNLGLPDLVAKYNTNNGAPKDFLPSPLHALLREW  
 TTYPESTVGTLMSKLRRELGRDAADLLLKASSVFKINLDGNGQEAYASSCNSGTSYNSI  
 SSVVSR

SEQID No:123

MWTPTEEEKYGVVICSFRGSVPQGLVLEIGETVQILEKCEGWYRGVSTKKPNVKGIFPA  
 NYIHLKKAIVSNRGQYETVVPLEDSIVTEVTATLQEWASLWKQLYVKHKVDLFYKLRHV  
 MNELIDLRRQLLSGHLTQDQVREVKRHITVRLDWGNEHLGLDLVPRKDFEVVDSQISV  
 SDLYKMHLSSRQSVQQSTSQVDTMRPRHGETCRMPVPHHFFLSLKSFTYNTIGEDTDV  
 FFSLYDMREGKQISERFLVRLNKNNGGPRNPEKIERMCALFTDLSSKDMKRDLYIVAHVIR  
 IGRMLLNDSSKKGPPHLHYRRPYGCAVLSILDVLQSLTEVKEEKDFVLKVYTCNNESEWS  
 QIHENIIRKSSAKYSAPSASHGLIISLQLLRGDMEQIRRENPMIFNRGLAITRKLGFDPVIM  
 PGDIRNDLYLTLEKGDFFERGGKSVQKNIEVTMYVLYADGEILKDCISLGSGEPNRSSYHS  
 FVLYHSNSPRWGEIILPIPIDRFRGSHLRFEFRHCSTKDKGEKKLFGFAFSTLMRDDGT  
 TLSDDIHELIVYKCDENSTFNNHALYLGLPCKEDYNGCPNIPSSLIFQRSTKESFFISTQ  
 LSSTKLTQNVDLLALLKWKAFPDRLMDVLGRLRHVSGEEIVKFLQDILDTLFVILDDNTEK  
 YGLLVFQSLVFIINLLRDIKYFHFRPVMDTYIQKHFA GALAYKELIRCLKWYMDCSAELIR

QDHIQEAMRALEYLFKFIVQSRILYSRATCGMEEEQFRSSIQELFQSIRFVLSLDSRNSET  
 LLFTQAALLNSFPTIFDELLQMFTVQEVAEFVRGTLGSMPTVHIGQSMDEVVKLQSIART  
 VDSRLFSFSESRRILLPVVLHHIHLHLRQQKELLICSGILGSIFSIVKTSSLEADVMEEVEM  
 MVESLLDVLLQTLLTIMSKSHAQEAVRGQRCPQCTAEITGEYVSCLLSLLRQMCDTHFQ  
 HLLDNFQSKDELKEFLLKIFCVFRNLMKMSVFPRDWMVMRLLTSNIIVTTVQYLSSALHK  
 NFTETDFDFKVVNSYFSLAVLFINQPSLQLEIITSAKRKKILDKYGDMRVMMAYELFSMW  
 QNLGEHKKIHFIPGMIGPFLGVTLVPQPEVRNIMIPIFHDMMDWEQRKNGNFKQVEAELID  
 KLDSMVSEGKGDESYRELFSLTQLFGPYPSLLEKVEQETWRETGISFVTSVTRLMERL  
 LDYRDCMKGEETENKKIGCTVNL MNFYKSEINKEEMYIRYIHKLCDMHLQAENYTEAAF  
 TLLLYCELLQWEDRPLREFLHYPSTEWQRKEGLCRKIIHYFNKGKSWFEFGIPLCRELA  
 CQYESLYDYQSLSWIRKMEASYDNIMEQQRLEPEFFRVGFYGRKFPFFLRNKEYVCR  
 GHDYERLEAFQQRMLSEFPQAVAMQHHPNHPDDAILQCDAAQYLQIYAVTPIPDYVDVLQ  
 MDRV PDRVKSFYRVNNVRKFRYDRPFHKGPKDKENEFKSLWIERTTLTLTHSLPGISR  
 WFEVERRELVEVSPL ENAIQVVENKNQELRSLISQYQHKQVHGNINLLSMCLNGVIDAA  
 VNGGIARYQEAFD KDKYINKHPGDAEKITQLKELMQEQVHVLGVGLAVHEKFVHPEMR  
 PLHKKLIDQFQMMRASLYHEFPGLDKLSPACSGTSTPRGNVLASHSPMSPESIKMTHR  
 HSPMNL MGTGRHSSSSSLSSHASSEAGNMVMLGDGSMGDAPEDLYHHMQLAYPNPRY  
 QGSVTNVSVLSSSSQASPSSSSLSSTHSAPSQMITSAPSSARGSPSLPDKYRHAREMML  
 LLPTYRDRPSSAMYPAAILENGQPPNFQRALFQQVVGACKPCSDPNLSVAEKGHYSLH  
 FDAFHHP LGDTPPALPARTLRKSPLHPIPASPTSPQSGLDGSNSTLSGSASSGVSSLSE  
 SNFGHSSEAPPRTDTMDSMPSQAWNADLEDPPYLPVHYSLSSESAVLDSIKAQPCRSH  
 SAPGCVIPQDPM DPPALPPKPYHPRLPALEHDEGVLLREETERPRGLHRKAPLPPGSA  
 KEEQARMAWEHGRGEQ

SEQID No:124

MAATFFGEVVKAPCRAGTEDEEEEEEGRRRETPEDREVRLQLARKREVRLRRQTKTSL  
 EVSLLEKYPCSKFIIAIGNNAVAFLSSFVMNSGVWEEVGC AKLWNEWCRTTDTTHLSST  
 EAF CVFYHLKSNPSVFLCQCSCYVAEDQQYQWLEKVFGSCPRKNMQITILTCRHVTDY  
 KTSESTGSLPSPFLRALKTNFKDSACCPLEQPNIVHDLPAAVLSYCQVWKIPAILYLC  
 YTDVMKLDLITVEAFKPILSTRSLKGLVKNIPQSTEILKKLMTTNEIQSNIYT

SEQID No:125

MSWVQATLLARGLCRAWGGTCGAALTGTSISQVPRRLPRGLHCSAAAHSSSEQSLVPS  
 PPEPRQRPTKALVPFEDLFGQAPGGERDKASFLQTVQKFAEHSVRKRGHIDFIYLALRK



MREYGVERDLAVYNQLLNIFPKEVFRPRNIIQRIFVHYPRQQEAGIIVLEQMENHGVMP  
 NKETEFLLIQIFGRKSYPMKLVRLLKLVFPRFMNVNPFVPRDLPQDPVELAMFGLRHM  
 EPDLSARVTIYQVPLPKDSTGAADPPQPHIVGIQSPDQQAALARHNPARPVFVEGPFSL  
 WLRNKCYYHILRADLLPPEEREVEETPEEWNLYYPMQLDLEYVRSGWDNYEFDINEV  
 EEGPVFAMCMAGAHDQATMAKWIQGLQETNPTLAQIPVVFRLAGSTRELQTSSAGLEE  
 PPLPEDHQEEDDNLQRQQQGGQS

SEQID No:126

MQAHELFRYFRMPELVDFRQCVTLPTNTLMGFGAFSRRLTTFWRPRHPKPLKPPWHL  
 SMQSVEVAGSGGARRSALLDSDEPLVYFYDDVTTLYEGFQRGIQVSNNGPCLGSRKP  
 DQPYEWLSYKQVAELSECIGSALIQKGFKTAPDQFIGIFAQNRPEWVIEQGCGFAYSMVI  
 VPLYDTLGNEAITIYVNKAELSLVFVDKPEKAKLLLEGVENKLIPGLKIIVVMDSYGSELVE  
 RGQRCGVEVTSMKAMEDLGRANRRKPKPPAPEDLAVICFTSGTTGNPKGAMVTHRNIV  
 SDCSAFVKATENTVNPCPDDTLISFLPLAHMFERVVECVMLCHGAKIGFFQGDIRLLMD  
 DLKVLQPTVFPVVPRLNRMFDRIFGQANTTVKRWLLDFASKRKEADVRSIGIIRNNSLW  
 DRLIFHKVQSSLGGRVRLMVTGAAPVSATVLTFLRAALGCQFYEGYGQTECTAGCCLT  
 MPGDWTTGHVGAPMPCNLIKLGWQLEEMNYMASEGEGEVCVKGPNVFQGYLKDPAK  
 TAEALDKDGWLHTGDIGKWLPNGTLKIIDRKKHIFKLAQGEYIAPEKIENIYMRSEPVAQV  
 FVHGESLQAFLIAIVVPDVETLCSWAQKRGFEGSFEELCRNKDVKKAILEDMVRLGKDS  
 GLKPFEQVKGITLHPELFSIDNGLLTPTMKAKRPELRNYFRSQIDDLYSIIKV

SEQID No:127

MPSASCDTLLDDIEDIVSQEDSKPQDRHFVRKDVVPKVRRRRNTQKYLQEEENSPPSDS  
 TIPGIQKIWIRTWGCSHNNSDGEYMAGQLAAYGYKITENASDADLWLLNSCTVKNPAED  
 HFRNSIKKAQEENKKIVLAGCVPQAQPRQDYLKGLSIIIGVQQIDRVVEVVEETIKGHSVR  
 LLGQKKDNGRRLGGARLDLPKIRKNPLIEIISISTGCLNACTYCKTKHARGNLASYPIDEL  
 VDRAKQSFQEGVCEIWLTSED TGAYGRDIGTNLPTLLWKLVEVIPEGAMLRLGMTNPPY  
 ILEHLEEMAKILNHPRVYAFLHIPVQSASDSVLMEMKREYCVADFKRVVDFLKEKVPGITI  
 ATDIICGFPGETDQDFQETVKLVEEYKFPSLFINQFYPRPGTPAAKMEQVPAQVKKQRT  
 KDLSRVFHSYSPYDHKIGERQQVLVTEESFDSKFYVAHNQFYEQVLVPKNPAFMGKMV  
 EVDIYESGKHFMKGQPVSDAKVYTPSISKPLAKGEVSGLTKDFRNLGNLQLSSGSHTS  
 AASQCDSASSRMVLPMPRLHQDCALRMSVGLALLGLLFAFFVKVYN

SEQID No:128

MGGTTSTRRTFEADENENITVVKGIRLSENVIDRMKESSPSGSKSQRYSGAYGASVS  
DEELKRRVAEELALEQAKKESEDQKRLKQAKELDRERAAANEQLTRAILRERICSEEER  
AKAKHLARQLEEKDRVLKKQDAFYKEQLARLEERSSEFYRVTTTEQYQKAAEEVEAKFK  
RYESHPCADLQAKILQCYRENTHTQTLKCSALATQYMHCNVNHAKQSMLEKGG

SEQID No:129

MALAAARLLPQFLHSRSLPCGAVRLRTPAVAEVRLPSATLCYFCRCRLGLGAALFPR SAR  
ALAASALPAQGSRWVPLSSPGLPAAFASFPACPQRSYSTEEKPQQHQKTKMIVLGFSN  
PINWVRTRIKAFLIWAYFDKEFSITEFSEGAKQAFAHVSKLLSQCKFDLLEELVAKEVLHA  
LKEKVTSLPDNHKNALANIDEIVFTSTGDISIYYDEKGRKFVNILMCFWYLTSANIPSETL  
RGASVFQVKLGNQNVETKQLLSASYEFQREFTQGVKPDWTIARIEH SKLLE

SEQID No:130

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNA  
ARRPNSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAACKAVRTRYISTELGI  
RQRLLVAVLTSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPI  
GHLHLALRHILLEQHGDDFDWFFLVPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFI  
GGEPTPGRYCHGGFGVLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGR CILDATGVG  
CTGDHEGVHYSHLELSPGEPVQEGDPHFERSALTAHPVRDPVHMYQLHKAFARAELE  
TYQEIQELQWEIQNTSHLAVDGDRAAAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSC  
ADGSPRCPLRGADRADVADVLTGTALEELNRRYHPALRLQKQQLVNGYRRFDPARGME  
YTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEILPVPYVTEASRLTVLLPLAAAERDLA  
PGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVAHADVFAPVKAHVAELEERRFPGAR  
VPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVLTPDFLNRCRMHAISGWQAFF  
PMHFQAFHPAVAPPQGPPELGRDTGRFDRQAASEACFYNSDYVAARGRLAAASEQ  
EEELLES LDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDLYHRCLQSVLEGL  
GSRTQLAMLLFEQEQQNST

SEQID No:131

MKLKLNKFLAYFLVSIAGLLYALVQLGQPCDCLPPLRAAAEQLRQKDLRISQLQAELRR  
PPPAPAQPPEPEALPTIYVVTPTYARLVQKAELVRLSQTLSLVPRLHWLLVEDAEGPTPL  
VSGLLAASGLLFTHLVVLTPKAQRLREGEPGWVHPRGVEQRNKALDWLRGRGGAVGG  
EKDPPPPGTQGVVYFADDDNTYSRELSEEMRWTRGVSVWPVGLVGGLRFEGPQVQD

GRVVGHTAWEPSRPFVDMAGFAVALPLLLDKPNAQFDSTAPRGHLESSLLSHLVDP  
KDLEPRAANCTRVLVWHTRTEKPKMKQEEQLQRQGRGSDPAIEV

SEQID No:132

MAAPRAGRAGWSLRAWRALGGIRWGRRPRLTPDLRALLTSGTSDPRARVTYGTSL  
WARLSVGVTEPRACLTSGTPGPRAQLTAVTPDTRTREASENSGTRSRAWLAVALGAG  
GAVLLLLWGGGRGPPAVLAAPSPPPASPRSQYNFIADVVEKTAPAVVYIEILDRHPFLG  
REVPISNGSGFVVAADGLIVTNAHVVADRRRRVRVRLLSGDTYEAVVTAVDPVADIATLRI  
QTKEPLPTLPLGRSADVRQGEFVAMGSPFALQNTITSGIVSSAQRPARDLGLPQTNVE  
YIQTDAAIDFGNSGGPLVNLDGEVIGVNTMKVTAGISFAIPSDRLREFLHRGEKKNSSSGI  
SGSQRRYIGVMMLTLSPSILAEQLREPSFPDVQHGVLIHKVILGSPAHRAGLRPGDVIL  
AIGEQMVQNAEDVYEAVRTQSQLAVQIRRGRETLTLYVTPEVTE

SEQID No:133

MTQLFLWEYGDLHLFGPNQRPAPCYDPCEAVLVESIPEGLDFPNASTGNPSTSQAWLG  
LLAGAHSSLDIASFYWTLTNNDTHTQEPSAQQGEEVLRQLQTLAPKGVNVRIAVSKPSG  
PQPQADLQALLQSGAQVRMVDQMQLTHGVLHTKFWVVDQTHFYLG SANMDWRS LTQ  
VKELGVVMYNC SCLARDLT KIFEAYWFLGQAGSSIPSTWPRFYDTRYNQETPMEICLNG  
TPALAYLASAPPPLCPSGRTPDLKALLNVVDNARSFIYVAVMNYLPTLEFSHPHRFWPAI  
DDGLRRATYERGKVRLLISCWGHSEPSMRAFLLSLAALRDNHTHSDIQVKLFVVPAD E  
AQARIPYARVNH NKYMVTERATYIGTSNWSGNYFTETAGTSLLVTQNGRGGLRSQLEAI  
FLRDWDSPYIHDLDTSADSVGNACRLL

SEQID No:134

MRYFLLRPETLFLLCISLALWSYFFHTDEVKTIVKSSRDAVKMVKGKVAEIMQNDR LGGL  
DVLEAEFSKTWEFKNHNNAVYSIQGRRDHMEDRFEVLTD LANKTHPSIFGIFDGHGGE  
GGIRGAALRFFPTLSTLQVQSGQLTGAPRWPLVFTRISERDLDPGLCRGGYARKGGG  
ALTSPLRPGGLRGADVLLLD SFVCGSSGSRR

SEQID No:135

MEKQPQNSRRGLAPREVPPAVGLLLIMALMNTLLYLCLDHFFIAPRQSTVDPTHCPYGH  
FRIGQMKNCS PWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALSQLTSLEMKD  
DFLHGLQMLKSLQGTHVVTLLGYCEDDNTMLTEYHPLGSLSNLEETLNLSKYQNVNTW  
QHRLELAMDYVSIINYLHHSPVGTRVMCD SNDLPKTL SQYLLTSNFSILANDLDALPLVN

HSSGMLVKCGHRELHGDFVAPEQLWPYGEDVPFHDDLMPHYDEKIDIWKIPDISSFLLG  
HIEGSDMVRFHFLFDIHKACKSQTPSERPTAQDVLETYQKVLDTLRDAMMSQAREML

SEQID No:136

MQRAGSSGGRGECDISGAGRLGLEEAARLSCAVHTSPGGGRRPGQAAGMSAKERPK  
GKVIKDSVTLLPCFYFVELPILASSVVSLEYFLELTDVFKPVHSGFSCYDRSLSMPIEPTQ  
EAIPFLMLLSLAFAGPAITIMVGEGILYCCLSKRRNGVGLPNINAGGCNFNNSFLRRAVRF  
VGVHVFGLCSTALITDIIQLSTGYQAPYFLTVCCKPNYTSLSNVSCKENSYIVEDICSGSDLT  
VINSGRKSFPSQHATLAFAAVYVSMYFNSTLTDSSKLLKPLLVFTFIICGIIICGLTRITQY  
KNHPVDVYCGFLIGGGIALYLGLYAVGNFLPSDESMFQHRDALRSLTDLNQDPNRLLSA  
KNGSSSDGIAHTEGILNRNRDASSLTNLKRANADVEITPRSPMGKENMVTFSNTLPRA  
NTPSVEDPVRRNASIHASMDSARSKQLLTQWKNKNESRKLSLQVIEPEPGQSPPRSIE  
MRSSEPSRVGVNGDHHGPGNQYLKIQPGAVPGCNNSMPGGPRVSIQSRPGSSQLV  
HIPEETQENISTSPKSSSARAKWLKAAEKTACNRSNSQPRIMQVIAMSKQQGVLLQSSP  
KNTGEGSTVSCTGSIRYKTLTDHEPSGIVRVEAHPENNRPIIQIPSTEGEGSGSWKWKAP  
EKGSLRQTYELNDLNDRDSESCESLKDSFGSGDRKRSNIDSNEHHHHGITTIRVTPVEGS  
EIGSETLSISSSRDSTLRRKGNILIPERSNSPENTRNIFYKGTSPTRAYKD

SEQID No:137

MLTTLKPFGSVSVESKMNNKAGSFFWNLRQFSTLVSTSRMTMLCCLGLCKPKIVHSNW  
NILNNFHNRMQSTDIIRYLFQDAFIFKSDVGFQTKGISTLTALRIERLLYAKRLFFDSKQSL  
VPVDKSDDELKKVNLNHEVSNEDVLTKETKPNRISSRKLSEECNSLSDVLDAFSKAPTF  
PSSNYFTAMWTIAKRLSDDQKRFEKRLMFSHPAFNQLCEHMMREAKIMQYKYLLFSLH  
AIVKLGIPQNTILVQTLLRVTQERINECDEICLSVLSTVLEAMEPCKNVHVLRTGFRILVDQ  
QVWKIEDVFTLQVVMKCIGKDAPIALKRKLEMKALRELDREFSVLNSQHMFEVLAAMNHR  
SLILLDECSKVVLNDNIHGCPRLRIMINILQSCKDLQYHNLDLKFGLADYVAATFDIWKFRKVL  
FILILFENLGFRPVGLMDLFMKRIVEDPESLNMKNILSILHTYSSLNHVYKCQNKEQFVEV  
MASALTGYLHTISSENLLDAVYSFCLMNYFPLAPFNQLLQKDIISELLTSDDMKNAYKLHT  
LDTCLKLDDTVYLRDIALSLPQLPRELPSSHTNAKVAEVLSSLLGGEGHFSKDVHLPHNY  
HIDFEIRMDTNRNQVLPLSDVDTTSATDIQRVAVLCVSRSAAYCLGSSHPRGFLAMKMRH  
LNAMEGFHVILVNNWEMDKLEMEDAVTFLKTKIYSVEALPVAAVNVQSTQ

SEQID No:138

RVYADAPAKLLLPPPAAWDLAVRLRGAEAAASERQVYSVTMKLLLLHPAFQSCLLLLTLLG



LWRTTPEAHASSLGAPASAAASFLQDLIHRYGEGDSLTLQQLKALLNHLDVGVGRGNVT  
 QHVQGHRLSTCFSSGDLFTAHNFSEQSRIGSSELQEFCTILQQLDSRACTSENQEN  
 EENEQTEEGRPSAVEVWGYGLLCVTVISLCSLLGASVVPFMKKTFYKRLLLYFIALAIGTL  
 YSNALFQLIPEAFGFNPLEDYYVSKSAVVFGGFYLFFFTEKILKILLKQKNEHHHGHSHYA  
 SESLPSKKDQEEGVMEKLQNGDLDHMIPQHCSSELDGKAPMVDEKVIVGSLSVQDLQA  
 SQSACYWLKGVRYSDIGTLAWMITLSDGLHNFIDGLAIGASFTVSVFQGISTSVAILCEEFF  
 PHELGDFFVILLNAGMSIQQALFFNFLSACCCYLGLAFGILAGSHFSANWIFALAGGMFLYI  
 SLADMFPENNEVCQEDERKGSILIPFIIQNLGLLTGFTIMVVLTMYSGQIQIG

SEQID No:139

MAAEWASRFWLWATLLIPAAAVYEDQVGKFDWRQQYVGKVKFASLEFSPGSKKLVVA  
 TEKNVIAALNSRTGEILWRHVDKGTAEGAVDAMLLHGQDVITVSNGGRIMRSWETNIGG  
 LNWEITLDSGSFQALGLVGLQESVRYIAVLKKTTLALHHLSSGHLKWVEHLPESDSIHYQ  
 MVYSYGSGVWVALGVVPFSHVNIKFNVEDGEIVQQVRVSTPWLQHLSGACGVVDEA  
 VLVCPDPSSRSLQTLALETEWELRQIPLQSLDLEFGSGFQPRVLPTQPNPVDASRAQFF  
 LHLSPSHYALLQYHYGTLSLLKNFPQTALVSFATTGEKTVAAVMACRNEVQKSSSSSEDG  
 SMGSFSEKSSSKDSLACFNQTYTINLYLVETGRRLDITTFSEQSGTRPERLYIQVFLK  
 KDDSVGYRALVQTEDHLLLFLQQLAGKVVLWSREESLAEVVCEMVDLPLTGAQAELE  
 GEFGKKADGLLGMFLKRLSSQLILLQAWTSHLWKMFYDARKPRSQIKNEINIDTLARDEF  
 NLQKMMVMVTASGKLFGISSSGTILWKQYLPNVKPDSSFKLMVQRTTAHFPHPPQCT  
 LLVKDKESGMSSLYVFNPFIKWSQVAPPVLKRPIQSLLLPVMDQDYAKVLLLIDDEYK  
 VTAFPATRNVLRLHELAPSIFFYLVDAAEQGRLCGYRLRKDLTTLSWELTIPPEVQRIV  
 KVKGKRSSEHVHSQGRVMGDRSVLYKSLNPNLLAVVTESTDAHHERTFIGIFLIDGVTG  
 RIIHSSVQKKAKGPVHIVHSENWVVYQYWNTKARRNEFTVLELYEGTEQYNATAFSSLD  
 RPQLPQVLQQSYIFPSSISAMEATITERGITSRHLLIGLPSGAILSLPKALLDPRRPEIPTE  
 QSREENLIPYSPDVQIHAERFINYNQTVSRMRGIYTAPSGLESTCLVVAYGLDIYQTRVY  
 PSKQFDVLKDDYDYVLISSVLFGLVFATMITKRLAQVKLLNRAWR

SEQID No:140

MAKVSELYDVTWEEMRDKMRKWREENSRNSEQIVEVGEELINEYASKLGDDIWIIYEQV  
 MIAALDYGRDDLALFCLQELRRQFPGSHRVKRLTGMRFEAMERYDDAIQLYDRILQEDP  
 TNAARKRKIAIRKAQGKNVEAIRELNEYLEQFVGDDQEAWEHLAEELYINEHDYAKAAFCL  
 EELMMTNPHNHLVCQQYAEVKYTQGGLENLELSRKYFAQALKLNNRNMRALFGLYMS

ASHIASNPKASAKTKKDNMKYASWAASQINRAYQFAGRSKKETKYSCLKAVEDMLETLOI  
TQS

SEQID No:141

MWSIGAGALGAAALALLANTDVFLSKPQKALEYLEDIDLKTLEKEPRTFKAKELWEKN  
GAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDFQPYFKGEI  
FLDEKKKFYGPQRRKMMFMGFIRLGWYNFFRAWNGGFSGNLEGEFGFILGGVFVVGSG  
GKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

SEQID No:142

MTLIEGVGDEVTVLFSVLACLLVLALAWVSTHTAEGGDPLPQPSGTPTPSQPSAAMAAT  
DSMRGEAPGAETPSLRHRGQAAQPEPSTGFTATPPAPDSPQEPLVLRKFLNDSEQVA  
RAWPHDTIGSLKRTQFPGREQQVRLIYQGQLLGDDTQTLGSLHLPNCVLHCHVSTRV  
GPPNPPCPPGSEPGPSGLEIGSLLLPLLLLLLLLLLWYCQIQYRPFPLTATLGLAGFTLLL  
SLLAFAMYRP

SEQID No:143

MASGSNWLSGVNVVLVMAYGSLVFVLLFIFVKRQIMRFAMKSRRGPHVPVGHNA PKDL  
KEEIDIRLSRVQDIKYEPQLLADDDARLLQLETQGNQSCYNYLYRMKALDAIRTSEIPFHS  
EGRHPRSLMGKNFRSYLLDLRNTSTPFKGVRKALIDTLLDGYETARYGTGVFGQNEYL  
RYQEALSELATAVKARIGSSQRHHQSAAKDLTQSPEVSPTTIQVTYLPSSQKSKRAKHF  
LELKSFKDNYNTLESTL

SEQID No:144

MTARGLALGLLLLLLLCPAQVFSQSCVWYGECEGIAYGDKRYNCEYSGPPKPLPKDGYDL  
VQELCPGFFFGNVSLCCDVRQLQTLKDNLQLPLQFLSRCPSCFYNLLNLFCELTCSPRQ  
SQFLNVTATEDYVDPVTNQTKTNVKELQYYVGQSFANAMYNACRDVEAPSSNDKALGL  
LCGKDADACNATNWIEYMFNKDNGQAPFTITPVFSDFPVHGMPEPMNNATKGCDDESVD  
EVTAPCSCQDCSIVCGPKPQPPPPPPAPWTILGLDAMYVIMWITYMAFLLVFFGAFFAWW  
CYRKRYFVSEYTPIDSNIAFSVNASDKGEASCCDPVSAAFEGCLRRLFTRWGSFCVRN  
PGCVIFFSLVFITACSSGLVFVRVTTNPVDLWSAPSSQARLEKEYFDQHFPGPFFRTEQLII  
RAPLTDKHIYQPYPSPGADVFPFGPPLDIQILHQVLDLQIAIENITASDNETVTLQDICLAPL  
SPYNTNCTILSVLNYFQNSHSVLDHKKGDDFFVYADYHHTFLYCVRAPASLNDTSLLHD  
PCLGTFGGPVFPWLVLGGYDDQNYNNATALVITFPVNNYYNDTEKLQRAQAWKEKEFIN

FVKNYKNPNLTISFTAERSIEDELNRESDSVFTVVISYAIMFLYISLALGHIKSCRRLVD  
 SKVSLGIAGILIVLSSVACSLGVFSYIGLPLTLIVIEVIPFLVLAVGVDNIFILVQAYQRDERL  
 QGETLDQQLGRVLGEVAPSMFLSSFSETVAFFLGALSVM PAVHTFSLFAGLAVFIDFLL  
 QITCFVSLLGLDIKRQEKNRLDIFCCVRGAEDGTSVQASESCLFRFFKNSYSPLLLKDW  
 MRPIVIAIFVGVLSFSIAVLNKVDIGLDQSL SMPDDSYMVDYFKSISQYLHAGPPVYFVLE  
 EGHDTSSKGGQNMVCGGMGCNND SLVQQIFNAAQLDNYTRIGFAPSSWIDDYFDWVK  
 PQSSCCRVDNITDQFCNASVVD PACVRCRPLTPEGKQRPQGGDFMRFLPMFLSDNPN  
 PKCGKGGHAAYSSAVNILLGHGTRVGATYFMTYHTVLQTSADFIDALKKARLIASNV TET  
 MGINGSAYRVFPYSVFYVFYEQYLTIIDDTIFNLGVSLGAIFLVTMVLLGCELWSAVIMCA  
 TIAMVLVNMFGVMWLWGISLNAVSLVNLV MSCGISVEFCSHITRAFTVSMKGSRVERAE  
 EALAHMGSSVFSGITLTKFGGIVVLAFAKSQIFQIFYFRMYLAMVLLGATHGLIFLPVLLSY  
 IGPSVNKAKSCATEERYKGTERERLLNF

SEQID No:145

MSGCGLFLRTTAAARACRGLVVSTANRRLLRTSPPVRAFAKELFLGKIKKKEVFPFPEV  
 SQDELNEINQFLGPVEKFFTEEVD SRKIDQEGKIPDETLEKLKSLGLFGLQVP EEEYGGGLG  
 FSNTMYSRLGEIISMDGSITVTLAAHQ AIGLKGIILAGTEEQKAKYLPKLASGEHIAAFCLT  
 EPASGSDAASIRSRATLSEDKKH YILNGSKVWITNGGLANIFTVFAKTEVVDSDG SVKDK  
 ITAFIVERDFGGVTNGKPEDKLGIRGSNTCEVHFENTKIPVENILGEVGDGFKVAMN ILNS  
 GRFSMGSVVAGLLKRLIEMTA EYACTRKQFNKRLSEFGLIQEKFALMAQKAYVMESMT  
 YLTAGMLDQPGFPDCSIEAAMVKVFSSEA AWQCVSEALQILGGLGYTRDYPYERILRDT  
 RILLIFEGTNEILRMYIALTGLQHAGRILTTRIHELKQAKVSTVMDTVGRRLRDSLGR TVDL  
 GLTGNHGVVHPSLADSANKFEENTYCFGR TVETLLLRFGKTIMEEQVLVKRVANILINLY  
 GMTAVLSRASRSIRIGLRNHDHEVLLANTFCVEAYLQNLFSLSQLDKYAPENLDEQIKKV  
 SQQILEKRAYICAHPLDRTC

SEQID No:146

LERRWRRRRREAGAGAEAAAGSARPLGRQAAAARGSSPEAGAAAMAESIIRVQSPDGV  
 KRITATKRETAATFLKKVAKEFGFQNGFSVYINRNKTGEITASSNKSLNLLKIKHGDLLF  
 LFPSSLAGPSSEMETSVP PGFKVFGAPNVVEDEIDQYLSKQDGKIYRSRDPQLCRHG PL  
 GKCVHCVPLEPFDEEDYLNHLEPPVKHMSFHAYIRKLTGGADKGKFVALENISCKIKSGC  
 EGHLPWPNGICTKCQPSAITLNRQKYRHVDNIMFENHTVADRFLDFWRKTGNQHFGYL  
 YGRYTEHKDIPLGIRAEVAAYEPPQIGTQNSLELLEDPKAEVVDEIAAKLGLRKVGWIFT  
 DLVSEDTRKGTVRYSRNKDTYFLSSEECITAGDFQNKHPNMCRLSPDGHFGSKFVTAV

ATGGPDNQVHFEGYQVSNQCMALVRDECLLPCKDAPELGYAKESSESSEQYVPDVFYKD  
 VDKFGNEITQLARPLPVEYLIIDITTTFPKDPVYTFSISQNPFPPIENRDVLGETQDFHSLAT  
 YLSQNTSSVFLDTISDFHLLLFLVTNEVMPLQDSISLLEAVRTRNEELAQTWKRSEQWA  
 TIEQLCSEYPHPLPRHPVAGAGEQPTLHSSPLPVVPWIPHPAASWQVPSAMQRVETRP  
 PCQARGRLR

SEQID No:147

MATAGGGSGADPGSRGLLRLLSFCVLLAGLCRGNSVERKIYIPLNKTAPCVRLLNATHQI  
 GCQSSISGDTGVIHVVEKEEDLQWVLTGDPNPPYMLLESKHFTRDLMKLGRTSRIA  
 GLAVSLTKPSPASGFSPSVQCPNDGFGVYSNSYGPEFAHCREIQWNSLGNGLAYEDFS  
 FPIFLEDENETKVIKQCYQDHNLSQNGSAPTFFPLCAMQLFSHMHAVISTATCMRRSSIQ  
 STFSINPEIVCDPLSDYNVWSMLKPINTTGTLKPDDRVAATRLDSRSFFWNVAPGAE  
 SAVASFVTQLAAAEALQKAPDVTTLPRNVMFVFFQGETFDYIGSSRMVYDMEKGKFPV  
 QLENVDSFVELGQVALRTSLELWMHTDPVSQKNESVRNQVEDLLATLEKSGAGVPAVI  
 LRRPNQSQPLPPSSLQRFLRARNISGVVLADHSGAFHNKYYQSIYDTAENINVSYPEWL  
 SPEEDLNFTVDTAKALADVATVLGRALYELAGGTNFSDTVQADPQTVTRLLYGFLIKAN  
 NSWFQSILRQDLRSYLGDGPLQHYIAVSSPTNTTYVVQYALANLTGTVVNLTREQCQDP  
 SKVPSENKDLYEYSWVQGPLHSNETDRLPRCVRSTARLARALSPAFELSQWSSTEYST  
 WTESRWKDIRARIFLIASKELELITLVGFGILIFSLIVTYCINAKADVLFIAPREPGAVSY

SEQID No:148

MPSAKQRGSKGGHGAASPSEKGAHPSGGADDVAKKPPPAPQQPPPPPPAPHPQQHPQ  
 QHPQNQAHGKGGHRRGGGGGGGGKSSSSSSSASAAAAAAAASSSASCSRRLGRALNFLF  
 YLALVAAAFAFGWCVHHVLEEVQQVRRSHQDFSRQREELGQGLQGVEQKVQSLQATF  
 GTFESILRSSQHKQDLTEKAVKQGESEVSRISEVLQKLQNEILKDLSDGIHVVKDARERD  
 FTSLENTVEERLTELTKSINDNIAIFTEVQKRSQKEINDMKAKVASLEESEGNKQDLKALK  
 EAVKEIQTSAKSREWDMEALRSTLQTMESDIYTEVRELVSLLKQEQQAFKEAADTERLAL  
 QALTEKLLRSEESVSRLPEEIRRLEEELRQLKSDSHGPKEDGGFRHSEAFEALQQKSQ  
 GLDSRLQHVEDGVLSMQVASARQTESLESLLSKSQEHEQRLAALQGRLEGLGSSEAD  
 QDGLASTVRSLGETQLVLYGDVEELKRSVGELPSTVESLQKVQEQQVHTLLSQDQAQAA  
 RLPPQDFLDRLSSLDNLKASVSQVEADLKMLRTAVDSLVAYSVKIETNENNLESAGLL  
 DDLRNDLDRLFVKVEKIHKEKV



SEQID No:149

MFRNQYDNDVTWSPQGRIHQIEYAMEAVKQGSATVGLKSKTHAVLVALKRAQSELAA  
 HQKKILHVDNHIGISIAGLTADARLLCNFMRQECLDSRFVFDRPLPVSRLVSLIGSKTQIP  
 TQRYGRRPYGVGLLIAGYDDMGPHIFQTCPSANYFDCRAMSIGARSQSARTYLERHMS  
 EFMECNLNELVKHGLRALRETLPAEQDLTTKNV SIGIVGKDLEFTIYDDDDVSPFLEGLE  
 ERPQRKAQPAQPADEPAEKADEPMEH

SEQID No:150

SSIGTGYDLSASTFSPDGRVFQVEYAMKA VENSSTAIGIRCKDGVVFGVEKLVLSKLYEE  
 GSNKRLFNVDHRHVGMAGVAGLLADARSLADIAREEASNFRSNFGYNIPLKHLADRVAMY  
 VHAYTLYSAVRPFGCSFMLGSYSVNDGAQLYMIDPSGVS YGYWGC AIGKARQA AKTEI  
 EKLQMKEMTCRDIVKEVAKIIVHDEVKDKAFELELSWVGELTNGRHEIVPKDIREEAEK  
 YAKESLKEEDESDDDNM

SEQID No:151

MSRRYDSRTTIFSPEGRLYQVEYAMEAIGHAGTCLGILANDGVLLAAERRNIHKLLDEVF  
 FSEKIYKLNEDMACSVAGITSDANVLTNELRLIAQRYLLQYQEPIPCQLVTALCDIKQAY  
 TQFGGKRPFVGSLLYIGWDKH YGFQLYQSDPSGNYGGWKATCIGNNSAAAVSMLKQD  
 YKEGEMTLKSALALAIKVLNKTMDVSKLSAEKVEIATLTRENGKTVIRVLKQKEVEQLIKK  
 HEEEEAKAEREKKEKEQKEKDK

SEQID No:152

MSRGSSAGFDRHITIFSPEGRLYQVEYAFKAINQGGLTSVAVRGKDCAVIVTQKKVPDK  
 LLDSSTVTHLKFITENIGCVMTGMTADSR SQVQRARYEAANWKYKYGYEIPVDMLCKRI  
 ADISQVYTQNAEMRPLGCCMILIGIDEEQGPQVYKCDPAGYYCGFKATAAGVKQTESTS  
 FLEKKVKKKFDWTFEQTVETAITCLSTVLSIDFKPSEIEVG VVTVENPKFRILTEAEID AHL  
 VALAERD

SEQID No:153

MLSSTAMYSAPGRDLGMEPHRAAGPLQLRFSPYVFNGGTILAIAGEDFAIVASDTRLSE  
 GFSIHTRDSPKCYKLTDKTVIGCSGFHGDCLTLTKIIEARLKMYKHSNNKAMTTGAIAAM  
 LSTILYSRRFFPYVYVNIIGGLDEEGKGAVYSFDPVGSYQRDSFKAGGSASAMLQPLLD  
 NQVGFKNMQNVEHVPLSLDRAMRLVKDVFISAAERDVYTG DALRICIVTKEGIREETVSL  
 RKD

SEQID No:154

MEYLIQIGPDYVLVASDRVAASNIVQMKDDHDKMFKMSEKILLLCVGEAGDTVQFAEYI  
QKNVQLYKMRNGYELSPTAAANFTRRNLDCLRSRTPYHVNLLLAGYDEHEGPALYYM  
DYLAALAKAPFAAHGYGAFLTLSILDYRYTPTISRERAVELLRKCLEELQKRFILNLPTFSV  
RIIDKNGIHDLDNISFPKQGS

SEQID No:155

MSIMSYNGGAVMAMKGKNCVAIAADRRFGIQAQMVTTFQKIFPMGDRLYIGLAGLATD  
VQTVAQRLKFRLNLYELKEGRQIKPYTLMSMVANLLYEKRFPGPYTEPVIAGLDPKTFKP  
FICSLDLIGCPMVTDDFVVS GTCAEQMYGMCESLWEPNMDPDHLFETISQAMLNAVDR  
DAVSGMGVIVHIIKDKITTRTLKARMD

SEQID No:156

MEAFSGSRGLWAGGPAPGQFYRIPSTPDSFMDPASALYRGPITRTQNPMVTGTSVLG  
VKFEGGVVIAADMLGSYGSLARFRNISRIMRVNNSTMLGASGDYADFQYLKQVLGQMVI  
DEELLGDGHSYSPRAIHSWLTRAMYSRRSKMNPLWNTMVIGGYADGESFLGYVDM LG  
VAYEAPSLATGYGAYLAQPLLREVLEKQPVLSQTEARDLVERCMRVLYYRDARSYNRF  
QTATVTEKGVEIEGPLSTETNWDIAHMISGFE

SEQID No:157

MALASVLERPLPVNQRGFFGLGGRADLLDLGPGSLSDGLSLAAPGWGVPEEPGIEM LH  
GTTTLAFKFRHGVIVAADS RATAGAYIASQTVKKVIEINPYLLGT MAGGAADCSFWERLL  
ARQCRIYELRNKERISVAAASKLLANMVYQYKGMGLSMGMTMICGWDKRGPGLYYVDSE  
GNRISGATFSVGSGSVYAYGVMDRGYSYDLEVEQAYDLARRAIYQATYRDAYS GGAVN  
LYHVREDGWIRVSSDNVADLHEKYSGSTP

SEQID No:158

MAATLLAARGAGPAPAWGPEAFTPDWESREVSTGTTIMAVQFDGGVVLGADSRTTTG  
SYIANRVTDKLTPIHDRIFCCRS GSAADTQAVADAVTYQLGFHSIELNEPPLVHTAASLFK  
EMCYRYREDLMAGIIIAGWDPQEGGQVYSVPMGGMMVRQSF AIGGSGSSYIYGYVDA  
TYREGMTKEECLQFTANALALAMERDGSSGGVIRLAAIAESGVERQVLLGDQIPKFAVA  
TLPPA

SEQID No:159

MGQSQSGGHGPGGGGKKDDKDKKKKKYEPPVPTRVGKKKKKTKGPDAASKLPLVTPHT  
 QCRLKLLKLERIKDYLLMEEEFIRNQEQMKNPLEEKQEEERSKVDDLRGTPMSVGTLEEII  
 DDNHAIVSTSVGSEHYVSILSFVDKDLLEPGCSVLLNHKVHAVIGVLMDDTDPLVTVMKV  
 EKAPQETYADIGGLDNQIQEIKESVELPLTHPEYYEEMGIKPPKGVILYGPPGTGKTLLAK  
 AVANQTSATFLRVVGSELIQKYLGDGPKLVRELFRVAEEHAPSIVFIDEIDAIGTKRYDSN  
 SGGEREIQRTMLELLNQLDGFDSRGDVKVIMATNRIETLDPALIRPGRIDRKIEFPLPDEK  
 TKKRIFIHTSRMTLADDVTLDDLIMAKDDLSGADIKAICTEAGLMALRERRMKVTNEDF  
 KSKKENVLYKKQEGTPEGLYL

SEQID No:160

MPDYLGAQQRKTKEDKDDKPIRALDEGDIALLKTYGQSTYSRQIKQVEDDIQQLLKIN  
 ELTGIKESDTGLAPPALWDLAADKQTLQSEQPLQVARCTKIINADSEDPKYIINVKQFAKF  
 VVDLSQVAPTDIEEGMRVGVDRNKYQIHIPLPPKIDPTVTMMQVEEKPDVTYSDVGGC  
 KEQIEKLREVVETPLLHPERFVNLGIEPPKGVLLFGPPGTGKTLCARAVANRTDACFIRVI  
 GSELVQKYVGEGARMVRELFEMARTKKACLIFFDEIDAIGGARFDDGAGGDNEVQRTM  
 LELINQLDGFDPGRNIKVLMATNRPDTLDPALMRPGRILDRKIEFSLPDLEGRTHIFKI HAR  
 SMSVERDIRFELLARLCPNSTGAEIRSVCTEAGMFAIRARRKATEKDFLEAVNKVIKSYA  
 KFSATPRYMTYN

SEQID No:161

MNLLPNIESPVTRQEKMATVWDEAEQDGIGEEVLKMSTEEIIQRTRLLDSEIKIMKSEVL  
 RVTHELQAMKDKIKENSEKIKVNKTLPYLVSNVIELLDVDPNDQEEDGANIDLDSQRKGK  
 CAVIKTSTRQTYFLPVIGLVDAEKLKPGDLVGVNKNDSYLILETLPTHEYDSRVKAMEVDER  
 PTEQYSDIGGLDKQIQELVEAIVLPMNHKEKFENLGIQPPKGVLMYGPPGTGKTLLARAC  
 AAQTKATFLKLAGPQLVQMFIDGAKLVRDAFALAKEKAPSIIFIDELDAIGTKRFDSEKA  
 GDREVQRTMLELLNQLDGFQPNQVVKVIAATNRVDILDPALLRSGRLDRKIEFPMPNEE  
 ARARIMQIHSRKMNVSPPDVNYEELARCTDDFNQAQCKAVCVEAGMIALRRGATELTHE  
 DYMEGILEVQAKKKANLQYYA

SEQID No:162

MEEIGILVEKAQDEIPALSVSRPQTGLSFLGPEPEDLEDLYSRYKKLQQELEFLEVQEEYI  
 KDEQKNLKKFLHAQEEVKRIQSIPLVIGQFLEAVDQNTAIVGSTTGSNYYVRILSTIDRE  
 LLKPNASVALHKHSNALVDVLPPEADSSIMMLTSDQKPDVMYADIGGMIDQKQEVREAV

ELPLTHFELYKQIGIDPPRGVLMYGPPGCGKTMLAKAVAHHTTAAFIRVVGSEFVQKYL  
 GEGPRMVRDVFR LAKENAPAIIFIDEIDAIATKRFDAQTGADREVQRILLELLNQMDGFD  
 QNVNVKVIMATNRADTLD PALLRPGR LDRKIEFPLPDRRQKRLIFSTITSKMNLSEEVDL  
 EDYVARPDKISGADINSICQESGMLAVRENRYIVLAKDFEKAYKTVIKKDEQEHEFYK

SEQID No:163

MALDGPEQMELEEGKAGSGLRQYYLSKIEELQLIVNDKSQNLRR LQAQRNELNAKVRL  
 REELQLLQEQGSYVGEVVRAMDKKKVLVKVHPEGKFVVDVDKNIDINDVTPNCRVALR  
 NDSYTLHKILPNKVDPLVSLMMVEKVPDSTYEMIGGLDKQIKEIKEVIELPVKHPELFEAL  
 GIAQPKGVL LYGPPGTGKTLLARAVAHHTDCTFIRVSGSELVQKFIGEGARMVRELFVM  
 AREHAPSIIFMDEIDSIGSSRLEGGSGGDSEVQRTMLELLNQLDGFEATKNIKVIMATNRI  
 DILDSALLRPGRIDRKIEFPPPNEEARLDILKIH SRKMNLTRGINLRKIAELMPGASGAEVK  
 GVCTEAGMYALRERRVHVTQEDFEMAVAKVMQKDSEKNMSIKKLWK

SEQID No:164

MADPRDKALQDYRKKLLEHKEIDGRLKELREQLKELTKQYEKSENDLKALQSVGQIVGE  
 VLKQLTEEFIVKATNGPRYVVG CRRQLDKSKLKPGRTRVALDMTTLTIMRYLPREVDPL  
 VYNMSHEDPGNVSYSEIGGLSEQIRELREVIELPLTNPELFQRVGIIPPKGCLLYGPPGT  
 GKTLLARAVASQLDCNFLKVVSSSIVDKYIGESARLIREMFNYARDHQPCIIFMDEIDAIG  
 GRRFSEGTSADREIQRTLME LLNQMDGFDTLHRVKMIMATNRPDTLD PALLRPGR LDR  
 KIHIDLPNEQARLDILKIHAGPITKHGEIDYEAIVKLSDGFNGADLRNVCTEAGMFAIRADH  
 DFVVQEDFMKAVRKVADSKKLESKLDYKPV

SEQID No:165

MITSAAGIISLLDEDEPQLKEFALHKLNAVVNDFWAEISESVDKIEVLYEDEGFRSRQFAA  
 LVASKVIFYHLGAFEESLNYALGARDLFNVNDNSEYVETIIAKCIDHYTKQCVENADLPEG  
 EKKPIDQRLEGIVNKMFRCLDDHKYKQAIGIALETRRLDVFEKTILESNDVPGMLAYSL  
 KLCMSLMQNKQFRNKVLRVLVKIYMNLEKPDFINVCQCLIFLDDPQAVSDILEKLVKEDN  
 LLMAYQICFDLYESASQQFLSSVIQNLRTVGTPIASVPGSTNTGTVP GSEKDSDSMETE  
 EKTSSAFVGKTPEASPEPKDQTLKMIKILSGEMAIELHLQFLIRNNNTDLMILKNTKDAVR  
 NSVCHTATVIANSFMHCGTTSDQFLRDNLEWLARATNWAKFTATASLGVIHKGHEKEAL  
 QLMATYLPKDTSPGSAYQEGGGLYALGLIHANHGGDIIDYLLNQLKNASNDIVRHGGSL  
 GLGLAAMGTARQDVYDLLKTNLYQDDAVTGEAAGLALGLVMLGSKNAQAIEDMVG YAQ  
 ETQHEKILRGLAVGIALV MYGRMEEADALIESLCRDKDPI LRRSGMYTVAMAYCGSGNN



KAIRRLHVAVSDVNDDVRSAAVESLGFILFRTPEQCPSVVSLLSESYNPHVRYGAAMA  
 LGICCAGTGNKEAINLLEPMTNDPVNYVRQGALIASALIMIQQTEITCPKVNQFRQLYSKV  
 INDKHDDVMAKFGAILAQGILDAGGHNVITISLQSRTGHTHMPSVVGVLVFTQFWFWFPL  
 SHFLSLAYTPTCVIGLNKDLKMPKVQYKSNCKPSTFAYPAPLEVPEKEKEKEKVSTAVLSI  
 TAKAKKKEKEKEKEKEEKEMEVDEAEKKEEKEKKEKEPEPNFQLLDNPARVMPAQLKVLT  
 MPETCRYQPFKPLSIGGIILKDTSEDIEELVEPVAAHGPKIEEEEQEPEPEPEFEYIDD

SEQID No:166

MAAAAVVEFQRAQSLLSTDREASIDILHSIVKRDIQENDEEAVQVKEQSILELGSLLAKTG  
 QAAELGGLLK YVRPFLNSISKAKAARLVRSLLDLFLDMEAATGQEVELCLECIEWAKSEK  
 RTFLRQALEARLVSLYFDTKRYQEALHLGSQLLRELKKMDDKALLVEVQLLESKTYHAL  
 SNLPKARAALTSARTTANAIYCPPKLQATLDMQSGIIHAAEEKDWKTAYSIFYEAFEGYD  
 SIDSPKAITSCLKYMLLCKIMLNTPEDEVQALVSGKLALRYAGRQTEALKCVAQASKNRSLA  
 DFEKALTDYRAELRDDPIISTHLAKLYDNLLEQNLIRVIEPFSRVQIEHISSLIKLSKADVER  
 KLSQMILDKKFHGGILDQGGVLIIFDEPPVDKTYEAALETIQNMSKVVDLSLYNKAKKLT

SEQID No:167

MADGGSERADGRIVKMEVDYSATVDQRLPECAKLAKKEGRLQEVIETLLSLEKQTRTASD  
 MVSTSRILVAVVKMCYEAKEDWLLNENIMLLSKRRSQLKQAVAKMVQQCCTYVEEITDL  
 PIKLRLIDTLRMVTEGKIYVEIERARLTKTTLATIKEQNGDVKEAASILQELQVETYGSMEKK  
 ERVEFILEQMRLCLAVKDYIRTQIISKKINTKFFQEENTEKLKLKYYNLMIQLDQHEGSYLS  
 ICKHYRAIYDTPCIQAESKWKQALKSVVLYVILAPFDNEQSDLVHRISGDKKLEEIPKYK  
 DLLKLFTTMELMRWSTLVEDYGMELRKGSLESPATDVFGSTEEGEKRWKDLKNRVVE  
 HNIRIMAKYYTRITMKRMAQLLDLSVDESEAFLSNLVVNKTIFAKVDRLAGIINFQRPKDP  
 NNLLNDWSQKLNSLMSLVNKTTHLIAKEEMIHNLQ

SEQID No:168

MKDVPGLQSQNSGPGQPAVWHRLLELYTKKLWHQLTLQVLDFVQDPCFAQGDGLI  
 KLYENFISEFEHRVNPLSLVEIILHVVRQMTDPNVALTFLEKTREKVKSSDEAVILCKTAIG  
 ALKLNIGDLQVTKETIEDVEEMLNNLPGVTSVHSRFYDLSSKYYQTIGNHASYYKDALRF  
 LGCVDIKDLPVSEQQERAFTLGLAGLLGEGVFNFGEMLMHPVLESRLRNTDRQWLIDTLY  
 AFNSGNVERFQTLKTAWGQQPDLAANEAQLLRKIQLLCLMEMTFTRPANHRQLTFEEIA  
 KSAKITVNEVELLMKALSVGLVKGSIDEVDKRVHMTWVQPRVLDLQQIKGMKDRLEF  
 WCTDVKSMEMMLVEHQAHDILT

SEQID No:169

MEEGGRDKAPVQPQQSPAAAPGGTDEKPSGKERRDAGDKDKEQELSEEDKQLQDEL  
 EMLVERLGEKDTSLYRPALEELRRQIRSSTTSMTSVPKPLKFLRPHYGKLKEIYENMAP  
 GENKRFAADIISVLAMTMSGERECLKYRLVGSQEELASWGHEYVRHLAGEVAKEWQEL  
 DDAEKVQREPLTLVKEIVPYNMAHNAEHEACDLLMEIEQVDMLEKDIDENAYAKVCLYL  
 TSCVNYVPEPENSALLRCALGVFRKFSRFPEALRLALMLNDMELVEDIFTSCKDVVVQK  
 QMAFMLGRHGVFLELSEDEVEEYEDLTEIMSNVQLNSNFLALARELDIMEPKVPDDIYKT  
 HLENNRFGGSGSQVDSARMNLASSFVNGFVNAAFQGDKLLTDDGNKWLYKNKDHGM  
 LSAAASLGMILLWDVDGGLTQIDKYLYSSEDIKSGALLACGIVNSGVRNECDPALALLS  
 DYVLHNSNTMRLGSIFGLGLAYAGSNREDVLTLLLPVMGDSKSSMEVAGVTALACGMIA  
 VGSCNGDVTSTILQTIMEKSETELKDTYARWLPLGLGLNHLGKGEAIEAILAALEVSEPF  
 RSFANTLVDVCAYAGSGNVLKVQQLHICSEHFDSKEKEEDKDKKEKKDKDKKEAPAD  
 MGAHQGVAVLGIALIAMGEEIGAEMALRTFGHLLRYGEPTLRRVPLALALISVSNPRLNI  
 LDTLSKFSHDADPEVSYNSIFAMGMVGSGTNNARLAAMLRLAQAQYHAKDPNNLFMVRL  
 AQGLTHLGKGTLTLCPYHSDRQLMSQVAVAGLLTVLVSF LDVRNIILGKSHYVLYGLVAA  
 MQPRMLVTFDEELRPLPVSVRVGQAVDVVGQAGKPKTITGFQTHHTTPVLLAHGERAEL  
 ATEEFLPVTPILEGFVILRKNPNYDL

SEQID No:170

MKQEGSARRRGADKAKPPPGGGGEQEPPPPPPAPQDVEMKEEAATGGGSTGEADGKTA  
 AAAAEHSQRELDTVTLEDIKEHV KQLEKAVSGKEPRFVLRLRMLPSTSRRLNHVLYK  
 AVQGGFFTSNNATRD FLLPFLEEPMDTEADLQFRPRTGKAASTPLLPEVEAYLQLLVVIFM  
 MNSKRYKEAQKISDDL MQKISTQNRRLDLVAAKCYYYHARVYEF LDKLDVVR SFLHAR  
 LRTATLRHDADGQATLLNLLLRNYLHYSLYDQAEKLVSKSVFPEQANNNEWARYLYYT  
 GRIKAIQLEYSEARRTMTNALRKAPQHTAVGFKQTVHKLLIVVELLLGEIPDRLQFRQPSL  
 KRSLMPYFLLTQAVRTGNLAKFNQVLDQFGEKFQADGTYTLIIRLRHNVIKTGVRMISLS  
 YSRISLADIAQKLQLDSPEDA EFIVAKAIRDGVIEASINHEKGYVQSKEMIDIYSTREPQLA  
 FHQRISFCLDIHNMSVKAMRFPPKSYNKDLESAEERREREQQDLEFAKEMAEDDDDSF  
 P

SEQID No:171

MVLESTMVCVDNSEYMRNGDFLPTRLQAQQDAVNIVCHSKTRSNPENNVGLITLANDC  
 EVLTTLTPTDGRILSKLHTVQPKGKITFCTGIRVAHLALKHRQGKNHKMRIIAFVGSPVED

NEKDLVKLAKRLKKEKVNVDIINFGEEEVNTEKLTAFVNTLNGKDGTGSHLVTVPVPPGPSL  
 ADALISSPILAGEGGAMLGLGASDFEFGVDPSADPELALALRVSMEEQRQRQEEEEARR  
 AAAASAAEAGIATTGTEDSDDALLKMTISQQEFGRTGLPDLSSMTEEEQIAYAMQMSLQ  
 GAEFGQAESADIDASSAMDTSEPAKEEDDYDVMQDPEFLQSVLENLPGVDPNNEAIRN  
 AMGSLASQATKDGKKDKKEEDKK

SEQID No:172

MLTFMASDSEEEVCDERTSLMSAESPTPRSCQEGRQGPEDGENTAQWRSQENEEDG  
 EEDPDYVCSGVPGRPPGLEEEELTKYGAKHVIMLFVPVTLCMIVVVATIKSVRFYTEKN  
 GQLIYTPFTEDTPSVGQRLNSVLNLTLMISVIVVMTIFLVVLYKYRCYKFIHGWLIMSSLM  
 LLFLFTYIYLGEVLKTYNVAMDYPTLLLTVWNFGAVGMVCIIHWKGPLVLQQAYLIMISAL  
 MALVFIKYLPEWSAWVILGAISVYDLVAVLCPKGPLRMLVETAQERNEPIFPALYSSAMV  
 WTVGMAKLDPSSQGALQLPYDPEMEEDSYDSFGEPSYPEVFEPPLTGYPGEELEEEE  
 ERGVKLGLGDFIFYSVLVGKAAATGSGDWNTTLACFVAILIGLCLTLLLLAVFKKALPALPI  
 SITFGLIFYFSTDNLVRPFMDTLASHQLYI

SEQID No:173

MAAKVFESIGKFGLALAVAGGVVNSALYNVDAGHRAVIFDRFRGVQDIVVGEGTHFLIP  
 WVQKPIIFDCRSRPRNPVITGSKDLQNVNITLRILFRPVASQLPRIFTSIGEDYDERVLPS  
 ITTEILKSVVARFDAGELITQRELVSQRQVSDDLTERAATFGLILDDVSLTHLTFGKEFTEAV  
 EAKQVAQQEAERARFVVEKAEQQKKAIIISAEGDSKAAELIANSLATAGDGLIELRKLEA  
 AEDIAYQLSRSRNITYLPAGQSVLLQLPQ

SEQID No:174

MPLAQLADPWQKMAVESPSDSAENGQQIMDEPMGEEEINPQTEEVSIKEIAITHHVKEG  
 HEKADPSQFELLKVLGQGSFGKVFLVKKISGSDARQLYAMKVLKKATLKVRDRVRRTKM  
 ERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDLFTRLSKEVMFTEEDVKFYLAELA  
 LALDHLHSLGIIYRDLKPENILLDEEGHIKLTDFGLSKESIDHEKKAYSFCGTVEYMAPEV  
 VNRRGHTQSADWWSFGVLMFEMLTGTLPFQKGDRKETMTMILKAKLGMPQFLSPEAQ  
 SLLRMLFKRNPANRLGAGPDGVEEIKRHSFFSTIDWNKLYRREIHPPFKPATGRPEDTF  
 YFDPEFTAKTPKDSPGIPPSANAHQLFRGFSFVAITSDDSQAMQTVGVHSIVQQQLHRN  
 SIQFTDGYEVKEDIGVGSYSVCKRCIHKATNMEFAVKIIDKSKRDPTEEIEILLRYGQHPNI  
 ITLKDVYDDGKYVYVVTELMKGGELLDKILRQKFFSEREASAVLFTITKTVEYLHAQGVV  
 HRDLKPSNILYVDESGNPESIRICDFGFAKQLRAENGLLMTPCYTANFVAPEVLKRQGY

DAACDIWSLGVLLYTMLTGYTPFANGPDDTPEEILARIGSGKFSLSGGYWNSVSDTAKD  
 LVSKMLHVDPHQRLTAALVLRHPWIVHWDQLPQYQLNRQDAPHLVKGAMAATYSALN  
 RNQSPVLEPVGRSTLAQRRGIKKITSTAL

SEQID No:175

SVTQPAGSVMGRWSLTASPVTLTSLMPMTAGPAAGKSSSSTSWDTVLTAITCASTVQ  
 LISTTLGASASGARMPTTCCSGTTVFLTALQDTMQREELVKNATPPAEPARAEDLSPAP  
 HVTPTSCCPTLAPAAPPASLGTILMTIMFASTQSQWSIEVGVDDHFLDLQQKTSLFKKV  
 WPHQDVCVSTTCNTHCGSCDSQASCTSCRDPNKVLLFGECQYESCAPQYYLDFSTNT  
 CKAADRVLINELLGLRVDRKEDNLMQTFFLECDWSCSACSGPLKTDCLQCMDGYVLQD  
 GACVEQCLSSFYQDSGLCKNCDSYCLQCQGPHECTRCKGPFLLLEAQCVCQECGKGYF  
 ADHAKHKCTACPQGCLQCXHRDRCHLCDHGGFFLKSGLCVYNCPGFSVHTSNETCSG  
 KIHTPSLHVNGSLILPIGSIKPLDFSLLNVQDQEGRVEDLLFHVVSTPTNGQLVLSRNGKE  
 VQLDKAGRFSWKDVNEKKVRFVHSKEKLRKGYLFLKISDQQFFSEPQLINIQAFSTQAP  
 YVLRNEVLHISRGERATITTQMLDIRDDDNPDVVEIIDPPLHGQLLQTLQSPATPIYQF  
 QLDELSRGLLHYAHDGSDSTSDVAVLQANDGHSFHNILFQVKTPQNDRGLQLVANSM  
 VWVPEGGMLQITNRILQAEAPGASAEIIYKITQDYPQFGEVLLVNMPADSPADEGQH  
 LPDGRTATPTSTFTQQDINEGIVWYRHSGAPAQSDSFRFEVSSASNAQTRLESHMFNIA  
 ILPQTPEAPKVSLEASLHMTAREDGLTVIQPHSLSFINSEKPSGKIVYNITLPLHPNQGIIE  
 HRDHPHSPIRYFTQEDINQGKVMYRPPPAAPHLQELMAFSFA

SEQID No:176

MSSQPAGNQTS PGATEDYSYGSWYIDEPQGGEELQPEGEVPSCHTSIPPGLYHACLA  
 SLSILVLLLLLAMLVRRRQLWPDCVRGRPGLPSPVDFLAGDRPRAVPAAVFMVLLSSLCL  
 LLPDEDALPFLTASAPSQDGKTEAPRGAWKILGLFYAALYYPLAACATAGHTAAHLLG  
 STLSWAHLGVQVWQRAECPQVPKIYKYYSLLASLPLLLGLGFLSLWYPVQLVRSFSRRT  
 GAGSKGLQSSYSEEYLRNLLCRKKLGSSYHTSKHGFLSWARVCLRHCITYTPQPGFHLP  
 LKLVLSATLTGTAIYQVALLLVGVVPTIQKVRAGVTDDVSYLLASFGIVLSEDKQEVELV  
 KHHLWALEVCYISALVLSCLLTFLVLMRSLVTHRTNLRALHRGAALDLSPLHRSPHPSRQ  
 AIFCWMSFSAYQTAFICLGLLVQQIIFFLGTTALAFLVLMPLVHGRNLLLFRSLESSWPFW  
 LTLALAVILQNMAAHWVFLETHDGHPQLTNRRVLYAATFLLFPLNVLVGAMVATWRVLL  
 SALYNAIHLGQMDLSLLPPRAATLDPGYYTYRNFLKIEVSQSHPAMTAFCSLLLQAQSL  
 PRTMAAPQDSL RPGEEDEGMQLLQTKDSMAKGARPGASRGRARWGLAYTLLHNPTL  
 QVFRKTALLGANGAQP



SEQID No:177

MERPWGAADGLSRWPHGLGLLLLLQLLPPSTLSQDRLDAPPPPAAPLPRWSGPIGVS  
 WGLRAAAAGGAFPRGGRWRRSAPGEDEECGRVRDFVAKLANNTHQHVFDDLGRGSVS  
 LSWVG DSTGVILVLTTFHVPLVIMTFGQSKLYRSEDYGKNFKDITDLINNTFIRTEFGMAI  
 GPENSGKVVLTAEVSGGSRGGRIFRSSDFAKNFVQTDLPFHPLTQMMYSPQNSDYLLA  
 LSTENGLWVSKNFGGKWEEIHKAVCLAKWGSDNTIFFTTYANGSCKADLGALELWRTS  
 DLGKSFKTIGVKIYSFGLGGRFLFASVMADKDTTRRIHVSTDQGD TWSMAQLPSVGQE  
 QFYSILAANDDMVFMHVDEPGDTGFGTIFTSDDRGIVYSKSLDRHLYTTTGGETDFTNV  
 TSLRGVYITSVLSEDNSIQTMITFDQGGRWTHLRKPENSECDATAKNKNECSLHIHAS  
 SISQKLNVPMAPLSEPNAVGIIVAHGSGVDAISVMVPDVYISDDGGYSWTKMLEGPHYY  
 TILDSGGIIVAIEHSSRPINVIKFSTDEGQCWQTYTFTTRDPIYFTGLASEPGARSMNISIWG  
 FTESFLT SQWVS YTIDFKDILERNCEEKDYTIWLAHSTDPE DYEDGCILGYKEQFLRLRK  
 SSMCQNGRDYVVT KQPSICLCSLEDFLCDFGYR PENDSKCVEQPELKGHDL EFCLYG  
 REEHLTTNGYRKIPGDKCQGGVNPVREV KDLKKKCTSNFLSPEKQNSKSN SVPIILAIVG  
 LMLVT VVAGVLIVKKYVCGGRFLVHRYSVLQQHAEANGVDGVDALDTASHTNKSGYHD  
 DSDEDLLE

SEQID No:178

MPAHLLQDDISSSYTTTTTITAPPSRVLQNGGDKLETMPLYLEDDIRPDIKDDIYDPTYKD  
 KEGPSPKVEYVWRNIILMSLLHLGALYGITLIPTCKFYTWLWGVFYYFVSALGITAGAHRL  
 WSHRSYKARLPLRLFLIIANTMAFQNDVYEW ARDHRAHHKFSETHADPHNSRRGFFFS  
 HVGWLLVRKHPAVKEKGSTLDLSDEAEKLV MFQRRYYKPGLLMMCFILPTLVPWYFW  
 GETFQNSVFVATFLRYAVVLNATWL VN SAAHLFGYR PYDKNISPRENILVSLGAVGEGF  
 HNYHHSFPYDYSASEYRWHINFTTFFIDCMAALGLAYDRKKVSKAAILARIKRTGDGNYK  
 SG

SEQID No:179

MAAAAPGN GRASAPRLLLLFLVPLLWAPA AAVRAGPDEDLSHRNKEPPAPAQQQLQPQPV  
 AVQGPEPARVEKIFT PAAPVHTNKEDPATQTNLGFIHAFVAAISVIIVSELGDKTFFIAAIM  
 AMRYNRLTVLAGAMLALGLMTCLSVLFGYATTVIPRVYTYVYSTVLFAIFGIRMLREGLK  
 MSPDEGQEELEE VQAELKKKDEEFQRTKLLNGPGDVETGTSITVPQKKWLHFISPIFVQ  
 ALTLTFLAEWGDRSQLTTIVLAAREDPYGVAVGGTVGHCLCTGLAVIGGRMIAQKISVRT  
 VTIIIGGIVFLAFAFSALFISPD SGF

SEQID No:180

MTSIHFVVHPLPGTEDQLNDRLREVSEKLNKYNLNSHPPLNVLEQATIKQCVVGPNHAA  
FLLEDGRVCRIGFSVQPDRLELGKPDNNDGSKLNSNSGAGRTSRPGRTSDSPWFLSG  
SETLGRLAGNTLGSRWSSGVGGSGGGSSGRSSAGARDSRRQTRVIRTGRDRGSGLL  
GSQPQPVIPASVIPEELISQAQVVLQGKSRSVIIRELQRTNLDVNLAVNNLLSRDDEDGD  
DGDDTASESYLPGEDLMSLLDADIHSAHPSVIIDADAMFSEDISYFGYPSFRRSSLSRLG  
SSRVLLLPLERDSELLRERESVLRLRERRWLDGASFDNERGSTSKEGEPNLDKKNTPV  
QSPVSLGEDLQWWPDKDGTKFICIGALYSELLAVSSKGEYQWKWSESEPYRNAQNP  
SLHHPRATFLGLTNEKIVLLSANSIRATVATENNKVATWVDETLSSVASKLEHTAQTYSE  
LQGERIVSLHCCALYTCAQLENSLYWWGVVPFSQRKKMLEKARAKNKKPKSSAGISSM  
PNITVGTQVCLRNNPLYHAGAVAFSISAGIPKVGVLMEVWNMNDSCRFQLRSPESLKN  
MEKASKTTEAKPESKQEPVKTEMGPPSPASTCSDASSIASSASMPYKRRRSTPAPKE  
EEKVNEEQWSLREVVFVEDVKNVPVGKVLKVDGAYVAVKFPGTSSNTNCQNSSGPDA  
DPSSLLQDCRLLRIDEHQVVKTTGGTPKVPDCFQRTPKKLCIPEKTEILAVNVDSKGVHAV  
LKTGNWVRYCIFDLATGKAEQENNFPTSSIAFLGQNERNVAIFTAGQESPIILRDGNGTIY  
PMAKDCMGGIRDPDWLDLPPISLGMGVHSLINLPANSTIKKKA AVIIMAVEKQTLMQHIL  
RCDYEACRQYLMNLEQAVVLEQNLQMLQTFISHRCDGNRNILHACVSVCFPTSNKETK  
EEEEAERSERNTFAERLSAVEAIAANAISVVSSNGPGNRAGSSSSSRSLRLREMMRRSLR  
AAGLGRHEAGASSSDHQDPVSPPIAPPSWVPDPPAMD PDGDIDFILAPAVGSLTTAATG  
TGQGPSTSTIPGPSTEPSVVESKDRKANAHFILKLLCDSVVLQPYLRELLSAKDARGMT  
PFMSAVSGRAYPAAITILETAQKIAKAEISSSEKEEDVFMGMVCPSGTNPDDSPLYVLCC  
NDTCSFTWTGAEHINQDIFECRTCGLLES LCCCTECARVCHKGHDCCLKRTSPTAYCD  
CWEKCKCKT LIAGQKSARLDLLYRLLTATNLVTL PNSRGEHLLLFLVQTVARQTVEHCQ  
YRPPRIREDRNRKTASPEDSDMPDHDLEPPRFAQLALERV LQDWNALKSMIMFGSQEN  
KDPLSASSRIGHLLPEEQVYLNQQSGTIRLDCFT HCLIVKCTADILLDDTLGLTVKELQN  
KYTPGRREEAIAVTMRFLRSVARV FVILSVEMASSKKKNNFIPQPIGKCKRVFQALLPYA  
VEELCNVAESLIVPVRMGIARPTAPFTLASTSIDAMQGSEELFSVEPLPPRPSSDQSSSS  
SQSQSSYIIRNPQQRRISQSQPVRGRDEEQDDIVSADVEEVEVEGVAGEEDHHDEQE  
EHGEENAEAEAGQHDEHDEDGSDMELDLLAAAE TESDSESNHSNQDNASGRRSVVTAA  
TAGSEAGASSVPAFFSEDDSQSNDSSDSDSSSSSQSDDIEQETFMLDEPLERTTNSSHA  
NGAAQAPRSMQWAVRNTQHQR AASTAPSSTSTPAASSAGLIYIDPSNLRRSGTISTSAA  
AAAAALEASNASSYLTSASSLARAYSIVIRQISDL MGLIPKYNHLVYSQIPAAVKLTYQDA  
VNLQNYVEEKLIPTWNWMVSIMDSTE AQLRYGSALASAGDPGHPNHPLHASQNSARR

ERMTAREEASLRTLEGRRRATLLSARQGMMSARGDFLNYALSLMRSHNDEHSDVLPV  
 LDVCSLKHVAYVFQALYWIKAMNQQTTLDTPLERKRTRELLELGIDNEDSEHENDDD  
 TNQSATLNDKDDDSLPAETGQNHPFFRRSDSMTFLGCIPPNPFVPLAEAIPLADQPHL  
 LQPNARKEDLFGRPSQGLYSSSASSGKCLMEVTVDNRNCLEVLPTKMSYAANLKNVMN  
 MQNRQKKEGEEQPVLPEETESSKPGPSAHDLAALQKSSLLAEIGLTESEGPPLTSFRPQ  
 CSFMGMVISHDMLLGRWRLSLELFGRVFMEDVGAEPGSILTELGGFEVKESKFRREME  
 KLRNQQSRLDSLEVDRDRDLLIQQTMRQLNNHFGRRCATTPMAVHRVKVTFKDEPGE  
 GSGVARSFYTAIAQAFLSNEKLPNLECIQNANKGTHTSMLQRLNRGERDRERERERE  
 MRRSSGLRAGSRRDRDRDFRRQLSIDTRPFRPASEGNPSDDPEPLPAHRQALGERLY  
 PRVQAMQPAFASKITGMELLESPAQLLLLLLASEDSLRRARVDEAMELIIAHGRENGADSIL  
 DLGLVDSSEKVQQENRKRHGSSRSVVDMDLDDTDDGDDNAPLFYQPGKRGFYTPRP  
 GKNTEARLNCFRNIGRILGLCLLQNELCPITLNRHVIVKLLGRKVNWHDFAFFDPVMYES  
 LRQLILASQSSDADAVFSAMDLAFAIDLCKEEGGGQVELIPNGVNIPVTPQNVYEYVRKY  
 AEHRMLVVAEQPLHAMRKGLLDVLPKNSLEDLTAEDFRLLVNGCGEVNVQMLISFTSFN  
 DESGENAEKLLQFKRWFWSIVEKMSMTERQDLVYFWTSSPSLPASEEGFQPMPSITIR  
 PPDDQHLPTANTCISRLYVPLYSSKQILKQKLLLAIKTKNFGFV

SEQID No:181

MATHGQTCARPMCIPPSYADLGKVARDIFNKGFGFGLVKLDVKTCSGVEFSTSGSS  
 NTDTGKVTGTLETKYKWCEYGLTFTEKWNTDNTLGTEIAIEDQICQGLKLTFTDFTFSPNT  
 GKKSGKIKSSYKRECINLGCDVDFDFAGPAIHGSAVFGYEGWLAGYQMTFDSAQSKLT  
 RNNFAVGRTGDFQLHTNVNDGTEFGGSIYQKVCEDLDTSVNLAWTSGTNCTRFGIAA  
 KYQLDPTASISAKVNNSSLIGVGYTQTLRPGVKLTLSALVDGKSINAGGHKVGLALELEA

SEQID No:182

MDSNTAPLGPSCPQPPAPQPQARSRLNATASLEQERSERPRAPGPQAGPGPGVRD  
 AAAPAEPQAQHTRSRRERADGTGPTKGDMEIPFEEVLERAKAGDPKAQTEVGKHLYQLA  
 GDTDEELNSCTAVDWLVLAQKQGRREAVKLLRRCLADRRGITSENEREVRQLSSETDL  
 ERAVRKAALVMYWKLNPKKKKQVAVAELENVGVNEHDGGAQPGPVPKSLQKQRR  
 MLERLVSSSESKNYIALDDFVEITKKYAKGVIPSSLFLQDDEDDDELAKSPEDLPLRLKV  
 VKYPLHAIMEIKEYLIDMASRAGMHWLSTIIPTHHINALIFFFIISNLTIDFFAFFIPLVIFYLSF  
 ISMVICTLKVFQDSKAWENFRTLTDLLRFEPNLDVEQAEVNFNGWNHLEPYAHFLLSVFF  
 VIFSFPISKDCIPCSELAVITGFFTIVTSYLSLSTHAEPYTRRALATEVTAGLLSLLPSMPL  
 NWPYLKVLGQTFITVPVGHVVLNVSVPCLLYVYLLYLFFRMAQLRNFKGTYCYLVPYLV

CFMWCELSVVILLESTGLGLLRASIGYFLFLFALPILVAGLALVGVLQFARWFTSLELTkia  
 VTVAVCSVPLLLRWWTKASFsvvgmvksltrssmvklilvwltaivlfcwfyvyrsegm  
 kvynstltwqqygalcgprawketnmartqilcshleghrvtwtgrfkyvrvtidn  
 saesainmlpffigdwmrcllygeaypacspgntstaeelcrlkllakhpchikkfdry  
 kfeitvgmpfssgadgsrsreeddvtkdivlrassefksvllslrqgsliefstilegrlg  
 skwpvfelkaisclncmaqlsptrrhvkiehdwrstvhgavkfafdffffpflsaa

SEQID No:183

MSGPLSLPLALSPPRLLLLLLLLSLLPVARASEAEHRLFERLFEDYNEIIRPVANVSDPVII  
 HFEVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKP  
 DIVLYNNAVGDfQVDDKTKALLKYTGEVTWIPPAIFKSSCKIDVTYFPFDYQNCTMKFGS  
 WSYDKAKIDLVLIGSSMNLKDYWESGEWAIKAPGYKHDIKYNCCEEIYPDITYSLYIRRL  
 PLFYTINLIIPCLLISFLTTLVLFYLPSDCGEKVTLCSVLLSLTVFLLVITETIPSTSLVIPLIGEY  
 LLFTMIFVTLsIVITVFLNVHYRTPTTHTMPSWVKTVFLNLLPRVMFMTRPTSNEGNAQ  
 KPRPLYGAELSNLNCFSRAESKGCKEGYPCQDGMCGYCHHRRIKISNFSANLTRSSSS  
 ESVDVLSLSALSPEIKEAIQSVKYIAENMKAQNEAKEEQKAQEIQQLKRKEKSTETSDQ  
 EPGL

SEQID No:184

MEKRETFVQAVSKELVGEFLQFVQLDKEASDPFSLNELLDLSRKQKEELWQRLKNLLT  
 DVLLESPVDGWQVVEAQGEDNMETEhGSKMRKSIEIIYAITSVILASVSVINESENYEALL  
 ECVIILNGILYALPESERKLQSSIQDLCVTWWEKGLPAKEDTGKTAfVMLLRRSLETKTG  
 ADVCRLWRIHQALYCFDYDLEESGEIKDMLLECFININYIKKEEGRRFLSCLFNWNINFIK  
 MIHGTIKNQLQGLQKSLMVYIAEIYFRAWKKASGKILEAIENDCIQDFMFHGIHLPRRSPV  
 HSKVREVLSYFHHQKKVRQGVEEMLYRlyKpILWRGLKARNSEVRSNAALLFVEAFPIR  
 DPNLHAiEMDSEIQKQFEELYSLLEDpYPMVRSTGILGVCKITSKYWEMMPPTILIDLLKK  
 VTGELAFDTSSADVRCsvfkCLPMILDNKLShPLLEQLLPALRYSLHDNSEKVRVAFVD  
 MLLKIKAVRAAKFWKICPMEHILVRLETDSRPVSRRLVSLIFNSFLPVNQPEEVWCERCv  
 TLVQMNHAAARRFYQYAHEHTACTNIAKLIHVIRHCLNACIQRAVREPPEDEEEEEDGRE  
 KENVTVLDKTLsvNDVACMAGLLEIIVILWKSIDRSMENNKEAKLYTINKFASVLPEYLKV  
 FKDDRCKIPLFMLMSFMPASAVPPFSCGVISTLRSREEGAVDKSYCTLLDCLCSWGQV  
 GHILELVDNWLPTeHAQAKSNTASKGRVQIHdTRPVKPELALVYIEYLLTHPKNRECLLS  
 APRKKLNHLLKALETskADLESLLQTPGGKPRGFSEAAAPRAFGlHCRLSIHLQHKFCS  
 EGKVYLSMLEDtGFWLESKILSFIQDQEEDYKLHRVIYQQIIQTYLTVCKDVVMVGLGD



HQFQMQLLQSRSLGIMQTVKGFFYVSLLLDILKEITGSSLIQKTDSDDEEVAMLLDTVQKVF  
QKMLECIARSFRKQPEEGLRLLYSVQRPLHEFITAVQSRHTDTPVHRGVLSTLIAGPVVE  
ISHQLRKVSDVEELTPPEHLSDLPPFSRCLIGIIKSSNVVRSFLDELKACVASNDIEGIVCL  
TAAVHIILVINAGKHKSSKVREVAATVHRKLKTFMEITLEEDSIERFLYESSSRTLGEELLNS

SEQID No:185

MAAAAVQGGRRSGGSGGCSGAGGASNCGTGSGRSGLLDKWKIDDKPVKIDKWDGSAV  
KNSLDDSAKKVLEKYKYVENFGLIDGRLTICTISCFFAIVALIWDYMHPPFESKPVLALC  
VISYFVMMGILTIYTSYKEKSIFLVAHRKDPTGMDPDDIWQLSSSLKRFDDKYTLKLTFS  
GRTKQQREAEFTKSIKFFDHSGTLVMDAYEPEISRLHDSLAIERKIK

SEQID No:186

MAVLRQLALLLWKNYTLQKRKVLVTVLELFLPLLFPGLIWLRLKIQSENVPNATIYPGQSI  
QELPLFFTFPPPGDTWELAYIPSHSDAAKTVTETVRRALVINMRVRGFPSEKDFEDYIRY  
DNCSSSVLAAVVFEHPFNHSKEPLPLAVKYHLRFSYTRRNYMWTQTGSFFLKETEGWH  
TTSLFPLFPNPGPRELTSPDGGGEPGYIREGFLAVQHAVDRAIMEYHADAATRQLFQRLT  
VTIKRFPYPPFIADPFLVAIQYQLPLLLLLLSFTYTALTIAHAVVQEKERRLKEYMRMMGLS  
SWLHWSAWFLLFFLFLLIAASFMTLLFCVKVKPNVAVLSRSDPSLVLAFLLCFAISTISFSF  
MVSTFFSKANMAAAFGGFLYFFTYIPYFFVAPRYNWMTLSQKLCSCLLSNVAMAMGAQ  
LIGKFEAKGMGIQWRDLLSPVNVDDDFCFGQVLGMLLLDVLYGLVTWYMEAVFPGQF  
GVPQPWYFFIMPSYWCGKPRAVAGKEEEDSDPEKALRNEYFEAEPEDLVAGIKIKHLSK  
VFRVGNKDRAAVRDLNLNLYEGQITVLLGHNGAGKTTTSLMLTGLFPPTSGRAYISGYEI  
SQDMVQIRKSLGLCPQHDILFDNLTVAEHLYFYAQLKGLSRQKCPEEVKQMLHIIGLEDK  
WNSRSRFLSGGMRRKLSIGIALIAGSKVLILDEPTSGMDAISRRAIWDLLQRQKSDRTIVL  
TTHFMDEADLLGDRIAIMAKGELQCCGSSLFLKQKYGAGYHMTLVKEPHCNPEDISQLV  
HHHVPNATLESSAGAELSFIIPRESTHREFGLFAKLEKKQKELGASFGASITTMEEVFLR  
VGKLVDSMDIQAIQLPALQYQHERRASDWAVDSNLCGAMDPSDGIGALIEEERTAVKL  
NTGLALHCQQFWAMFLKKAAYSWREWKMVAAQVLVPLTCVTLALLAINYSSELFDDPM  
LRLTLGEYGRTVVPFSVPGTSQLGQQQLSEHLKDALQAEGQEPREVLGDLEEFIFRASV  
EGGGFNERCLVAASFRDVGERTVVNALFNQAYHSPATALAVVDNLLFKLLCGPHASIV  
VSNFPQPRSAALQAADQFNEGRKGFIDIALNLLFAMAFLASTFSILAVSERAVQAKHVQF  
VSGVHVASFWSALLWDLISFLIPSLLLLTVFKAFDVRAFTRDGHMADTLLLLLLLYGWAIL  
PLMYLMNFFFLGAATAYTRLTIFNILSGIATFLMVTIMRIPAVKLEELSKTLDHVFLVLPNH  
CLGMAVSSFYENYETRRYCTSSSEVAAHYCKKYNIQYQENFYAWSAPGVGRFVASMAA

SGCAYLILLFLIETNLLQRLRGILCALRRRRTLTELYTRMPVLPEDQQDVADERTRILAPSP  
 DSSLHTPLIIKELSKVYEQRVPLLAVDRLSLAVQKGECFGLLGFNAGKTTTTFKMLTGEE  
 SLTSGDAFVGGHRISSDVGKVRQRIGYCPQFDALLDHMTGREMLVMYARLRGIPERHI  
 GACVENTLRGLLLEPHANKLVRTYSGGNKRKLSTGIALIGEPAVIFLDEPSTGMDPVARR  
 LLWDTVARARESGKAIITSHSMEECEALCTRLAIMVQQGQFKCLGSPQHLKSKFGSGYSL  
 RAKVQSEGQQEAELEEFKAFVDLTFPGSVLEDEHQGMVHYHLPGRDLSWAKVFGILEKA  
 KEKYGVDDYSVSQISLEQVFLSFAHLQPPTAEAGR

SEQID No:187

MAQALPWLLLWMGAGVLPAGHTQHGIRLPLRSGLGGAFLGLRLPRETDEEPEEPGRR  
 GSFVEMVDNLRGKSGQGYVEMTVGSPQTLNILVDTGSSNFAVGAAPHPFLHRYQQ  
 RQLSSTYRDLRKGVYVPYTQGKWEDELGTDLVSIPHGPNTVRANIAAITESDKFFINGS  
 NWEGLGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAGFPLNQSEVLASVGG  
 SMIIGGIDHSLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTN  
 LRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGEQLVCWQAGTTPWNIFPVISLYLMGEVT  
 NQSFRTILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRARKRI  
 GFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLP  
 LCLMVCQWRCLRCLRQQHDDFADDISLLK

SEQID No:188

MSEADGLRQRRPLRPQVVTDDDGAPEAKDGSSFSGRVFRVTFLMLAVSLTVPLLGA  
 MMLLESPIDPQPLSFKEPPLLLGVLHPNTKLRQAERLFENQLVGPESIAHIGDVMFTGTA  
 DGRVVKLENGEIIETIARFGSGPCKTRDDEPVCGRPLGIRAGPNGTLFVADAYKGLFEVN  
 PWKREVKLLLSSETPIEGKNMSFVNDLTVTQDGRKIYFTDSSSKWQRRDYLLLVMEGT  
 DDGRLLEYDTVTREVKVLLDQLRFPNGVQLSPAEDFVLVAETTMARIRRVYVSGLMKG  
 GADLFVENMPGFPDNIRPSSSGGYWVGMSTIRPNPGFSMLDFLSERPWIKRMIFKLFS  
 QETVMKFVPRYSLVLELSDSGAFRRSLHDPDGLVATYISEVHEHDGHLYLGSFRSPFLC  
 RLSLQAV

SEQID No:189

MLKVTVPSCSASSCSSVTASAAPGTASLVPDYWIDGSNRDALSDFFEVESELGRGATSI  
 VYRCKQKGTQKPYALKVLKKTVDKKIVRTEIGVLLRLSHPNIIKLKEIFETPTEISLVLELVT  
 GGELFDRIVEKGYYSERDAADAVKQILEAVAYLHENGIVHRDLKPENLLYATPAPDAPLK  
 IADFGLSKIVEHQVLMKTVCGTPGYCAPEILRGCAYGPEVDMWSVGIITYILLCGFEPFY

DERGDQFMFRRILNCEYYFISPWWDEVSLNAKDLVRKLIVLDPKKRLTTFQALQHPWVT  
 GKAANFVHMDTAQKKLQEFNARRKLKAAVKAVVASSRLGSASSSHGSIQESHKASRDP  
 SPIQDGNEDMKAIPERGEKIQQDGAQAQAAVKGAQAELMKVQALEKVKGADINAEAPKMOV  
 PKAVEDGIKVADLEEEGLAEEKLKTVEEAAAPREGQGSSAVGFVPPQDQVILPEY

SEQID No:190

MSSSEEVSWISWFCGLRGNEFFCEVDEDYIQDKFNLTGLNEQVPHYRQALDMILDLEP  
 DEELEDNPNQSDLIEQAEMLYGLIHARYILTNRGIAQMLEKYQQGDFGYCPRVYCENQ  
 PMLPIGLSDIPGEAMVKLYCPKCMDVYTPKSSRHHHTDGAYFGTGFPHMLFMVHPEYR  
 PKRPANQFVPRLYGFKIHPMAYQLQLQAASNFKSPVKTIR

SEQID No:191

MWQLWASLCCLLVLANARSRPSFHPVSDELVNYVNKRNTTWQAGHNFYNVDMSYLKR  
 LCGTFLGGPKPPQRMFTEDLKLPASFDAREQWPQCPTIKEIRDQGSCGSCWAFGAV  
 EAISDRICHTNAHVSVEVSAEDLLTCCGSMCGDGCNGGYPAEAWNFWTRKGLVSGGL  
 YESHVGCRPYSIPPCEHHVNGSRPPCTGEGDTPKCSKICEPGYSPTYKQDKHYGYNSY  
 SVSNSEKDIMAEIYKNGPVEGAFSVYSDFLLYKSGVYQHVTGEMMGGHAIRILGWGVE  
 NGTPYWLANSWNTDWGDNGFFKILRGQDHCGIESEVVAGIPRTDQYWEKI

SEQID No:192

MMRQAPTARKTTTTRRPKPTRPASTGVAGASSSLGPSGSASAGELSSSEPSTPAQTPLA  
 APIIPTPVLTSPGAVPPLPSPSKEEEGLRAQVRDLEEKLETLRKRAEDKAKLKELEKHKI  
 QLEQVQEWKSKMQEQQADLQRRRLKEARKEAKEALEAKERYMEEMADTADAIEMATLD  
 KEMAEERAESLQQEVEALKERVDELTTDLLEILKAEIEEKGS DGAASSYQLKQLEEQNAR  
 LKDALVRMRDLSSSEKQEHVKLQKLMEKKNQELEVVRQQRERLQEELSQAESTIDELK  
 EQVDAALGAEEMVEMLTDRNLNLEEKVRELRETVGDLEAMNEMNDELQENARETELEL  
 REQ LDMAGARVREAQKRVEAAQETVADYQQTIKKYRQLTAHLQDVNREL TNQQEASV  
 ERQQQPPPETFD FKKIFAETKAHAKAIEMELRQMEVAQANRHMSLLTAFMPDSFLRPG  
 GDHDCVLVLLLMPRLICKAELIRKQAQEKFELSENCSERPGLRGAAGEQLSFAAGLVYS  
 LSLQATLHRYEHALSQCSVDVYKKVGS LYPEMSAHERSLDFLIELLHKDQLDET VNVE  
 PLTKAIKYYQHLYSIHLAEQPEDCTMQLADHIKFTQSALDCMSVEVGRLRAFLQGGQEA  
 TDIALLLRDLETSCSDIRQFCKKIRRRMPGTDAPGIPAALAFGPQVSDTLLDCRKHLTWV  
 VAVLQEVA AAAAAQLIAPLAENEGLLVAALEELAFKASEQIYGTPSSSPYECLRQSCNILIS  
 TMNKLATAMQEGEYDAERPPSKPPPVELRAAALRAEITDAEGLGLKLEDRETVIKELKK

SLKIKGEELSEANVRLSLLEKKLDSAAKDADERIEKVQTRLEETQALLRKKEKEFEETMD  
 ALQADIDQLEAEKAELKQRLNSQSKRTIEGLRGPPPSGIATLVSGIAGEEQQRGAIPGQA  
 PGSVPGPGLVKDSPLLLQQISAMRLHISQLQHENSILKGAQMKASLASLPPLHVAKLSHE  
 GPGSELPAGALYRKTSQLETLNQLSTHTHVVDITRTSPAAKSPSAQLMEQVAQLKSLS  
 DTVEKLDKDEVKTVSQRPGATVPTDFATFPSSAFLRAKEEQDDTVYMGKVTFSCAA  
 GFGQRHRLVLTQEQLHQLHSRLIS

SEQID No:193

MGKGGNQGEAAEREVSPTFSWEEIQKHNLRTDRWLVIDRKVYNITKWSIQHPGGQ  
 RVIGHYAGEDATDAFRAFHPDLEFVGKFLKPLLIGELAPEEPSQDHGKNSKITEDFRALR  
 KTAEDMNLFKTNHVFFLLLLAHIIALESIAWFTVFYFGNGWIPTLITAFVLATSQAQAGWL  
 QHDYGHLSVYRKPKWNHLVHKFVIGHLKGASANWWNHRHFQHHAKPNIFHKDPDVNM  
 LHVFLVGEWQPIEYGKKKLKYPYNHQHEYFFLIGPPLLIPMYFQYQIIMTMIVHKNWVDL  
 AWAVSYYIRFFITYIPFYGILGALLFLNFIRFLESHWFVWVTQMNHIVMEIDQEAYRDWFS  
 SQLTATCNVEQSFFNDWFSGHLNFQIEHHLFPTMPRHNHFKIAPLVKSLCAKHGIEYQE  
 KPLLRAALLDIIRSLKKSGKLWLDAYLHK

SEQID No:194

MASLDRVKVLVLGDSGVGKSSLVHLLCQNQVLGNPSWTVGCSVDVRVHDYKEGTPEE  
 KTCYIELWDVGGSVGSASSVKSTRAVFYNSVNGIIFVHDLTNKKSSQNLRRWSLEALNR  
 DLVPTGVLVTNGDYDQEQFADNQIPLLVIGTKLDQIHETKRHEVLTTTAFLAEDFNPEEIN  
 LDCTNPRYLAAGSSNAVKLSRFFDKVIEKRYFLREGNQIPGFPDRKRFGAGTLKSLHYD

SEQID No:195

MNNHVSSKPSTMKLKHTINPILLYFIHFLISLYTILTYIPFYFFSESREQESNRIKAKPVNSK  
 PDSAYRSVNSLDGLASVLYPGCDTLDKVFTYAKNKFKNKRLLGTTREVLNEEDEVPNG  
 KIFKKVILGQYNWLSYEDVFVRAFNFNGNGLQMLGQKPKTNIAIFCETRAEWMIAAQACF  
 MYNFQLVTLYATLGGPAIVHALNETEVTNIITSKELLQTKLKDIVSLVPRLRHIITVDGKPPT  
 WSDFPKGIIVHTMAAVEALGAKASMENQPHSKPLPSDIAVIMYTSGSTGLPKGVMISHS  
 NIIAGITGMAERIPELGEEDVYIGYLPLAHVLELSAELVCLSHGCRIGYSSPQTLADQSSKI  
 KKGSKGDTSMKPTLMAAVPEIMDRIYKNVMNKVSEMSSFQRNLFILAYNYKMEQISKG  
 RNTPLCDSFVFRKVRSLGGINRLLCGGAPLSATTQRFMNICFCCPVGQGYGLTESAG  
 AGTISEVWDYNTGRVGAPLVCCEIKLKNWEEGGYFNTDKPHPRGEILIGGQSVTMGY  
 KNEAKTKADFSEDENGQRWLCTGDIGEFEPDGCLKIIDRKKDLVKLQAGEYVSLGKVEA



ALKNLPLVDNICAYANSYHSYVIGFVVPNQKELTELARKKGLKGTWEELCNSCEMENEV  
LKVLSEAAISASLEKFEIPVKIRLSPEPWTPETGLVTDAFKLKRKELKTHYQADIERMYGR  
K

SEQID No:196

MKLKLNVLTIILLPVHLLITIYSALIFIPWYFLTNAKKKNAMAKRIKAKPTSDKPGSPYRSVT  
HFDSLAVIDIPGADTLDKLFDAVSKFGKKDSLGTREILSEENEMQPNGKVFKKLILGNY  
KWMNYLEVNRNRRVNNFGSGLTALGLKPKNTIAIFCETRAEWMIAAQTCFKYNFPLVTLYA  
TLGKEAVVHGLNESEASYLITSVELLESKLKTALLDISCVKHIIYVDNKAINKAEYPEGFEIH  
SMQSVEELGSPENLGIPPSRPTPSDMAIVMYTSGSTGRPKGVMHHSNLIAGMTGQ  
CERIPGLGPKDTYIGYLPLAHVLELTAEISCFTYGCRIGYSSPLTSDQSSKIKKGSKGDC  
TVLKPTLMAAVPEIMDRIYKNVMSKVQEMNYIQKTLFKIGYDYKLEQIKKGYDAPLCNLLL  
FKKVKALLGGNVRMMLSGGAPLSPQTHRFMNVCFCPIGQGYGLTESCGAGTVTEVT  
DYTTGRVGAPLICCEIKLDWQEGGYTINDKPNPRGEIVIGGQNISMGYFKNEEKTAEDY  
SVDENGQRWFCTGDIGEFHPDGCLQIIDRKKDLVKLQAGEYVSLGKVEAALKNCPLIDNI  
CAFAKSDQSYVISFVVPNQKRLTLLAQKQGVGTWVDICNNPAMEAEILKEIREAANAM  
KLERFEIPIKVRLSPEPWTPETGLVTDAFKLKRKELRNHYLKDIERYGK

SEQID No:197

MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPTGPEVQTPKPSDADWDDLWDQFDE  
RRYLNAKKWRVGDDPYKLYAFNQRESERISSNRAIPDTRHLSVLNRTPTHLIREILVDDF  
SNDDPDDCKQLIKLPVKCLRNNERQGLVRSRIRGADIAQGTTLTFLDSHCEVNRDWLQP  
LLHRVKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWSLHFQWEQLSPEQKARRLDP  
TEPIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGGENFEISFRVWMCGGSLEIVPCSRV  
GHVFRKKHPYVFPDGNANTYIKNTKRTAEVWMDEYKRYYYAARPFALERPFGNVESRL  
DLRKNLRCQSFKWYLENIYPELSIPKESSIQKGNIRQRQKCLESQANGTTGSSGQRPAG  
GTSEIWVQKPRVRNRRHAAPQGFDPGAKPSQHWRRPEHPAAE

SEQID No:198

MFFSMGFIVAVKGKIASPLEAPVFVAAPHSTFFDGIACVVAGLPSMVSARNENAQVPLIGR  
LLRAVQPVLSRVDPDSRKNTINEIIRTTSGGEWPQILVFPEGTCCTNRSCLITFKPGAFI  
PGVPVQPVLLRYPNKLDTVTWQGYTFIQLCMLTFCQLFTKVEVEFMPVQVPNDEEK  
NDPVLFANKVRNLMAEALGIPVTDHTYEDCRLMISAGQLTLPMEAGLVEFTKISRKLKLD  
WDGVRKHLDEYASIASSSKGGRIIEFAKYLKLPVSDVLRQLFALFDRNHDGSIDFREY

VIGLAVLCNPSNTEEEIIQVAFKLFDVDEDGYITEEEFSTILQASLGVPDLDVSGLFKEIAQG  
 DSISYEEFKSFALKHPEYAKIFTTYLDLQTCHVFSLPKEVQTTPSTASNKVSPEKHEEST  
 SDKKDD

SEQID No:199

MRPRRPHQIADLFRPKDQIAYSDTSPFLILSEASLADLNSRLEKKVKATNFRPNIVISGCD  
 VYAEDSWDELLIGDVELKRVMACSRCILTTVDPDTGVMSRKEPLETLKSYRQC DP SERK  
 LYGKSPLFGQYFVLENPGTIKVGDPVYLLGQ

SEQID No:200

MSSFYGYRTLTVLFTLICCPGSDEKVFVHVRPKKLAVEPKGSLEVNCSTTCNQPEVGG  
 LETSLNKILLDEQAQWKHYLVSNISHDTV LQCHFTCSGKQESMNSNVSVYQPPRQVILT  
 LQPTLVAVGKSFTIECRVPTVEPLDSLTLFLFRGNETLHYETFGKAAPAPQEATATFNST  
 ADREDGHRNFSCLAVLDLMSRGGNIFHKHSAPKMLEIYEPVSDSQMVIIVTVVSVLLSLF  
 VTSVLLCFIFGQHRLRQQRMGTYGVRAAWRRLPQA FRP

SEQID No:201

MDTEGFGELLQQAELAAETEGISELPHVERN LQEIQQAGERLRSRTLTRTSQETADV K  
 ASVLLGSRGLDISHISQRLESLSAATTFEPLPVKDTDIQGFLKNEKDNALLSAIEESRKR  
 TFGMAEEYHRESMLVEWEQVKQRILHTLLASGEDALDFTQESEPSYISDVGPGRSSL  
 DNIEMAYARQIYIYNEKIVNGHLQPNLVDLCASVAELDDKSISDMWTMVKQMTDVLLTPA  
 TDALKNRSSVEVRMEFVRQALAYLEQSYKNYTLTVFGNLHQAQLGGVPGTYQLVRSF  
 LNIKLPAPLPGLQDGEVEGHPVWALIYYCMRCGDLLAASQVVNRAQHQLGEFKTW FQE  
 YMNSKDRRLSPATENKLRLHYRRALRNNTDPYKRAVYCIIGRCDVTDNQSEVADKTED  
 YLWLKLNQVCFDDDGTSSPQDRLTLSQFQKQLLEDYGESHFTVNQQPFLYFQVLFLTA  
 QFEAAVAFLFRMERLRCHAVHVALVLFELKLLKSSGQSAQLLSHEPGDPPCLRRNLNFV  
 RLLMLYTRKFESTDPREALQYFYFLRDEKDSQGENMFLRCVSELVIESREFDMILGKLE  
 NDGSRKPGVIDKFTSDTKPIINKVASVAENKGLFEEAAKLYDLAKNADKVLELMNKLLSP  
 VVPQISAPQSNKERLKNMALSIAERYRAQGISANKFVDSTFYLLLDLITFFDEYHSGHIDR  
 AFDIIERLKLVLPLNQESVEERVA AFRNFSDEIRHNLSEVLLATMNILFTQFKRLKGTSPSS  
 SSRPQRVIEDRDSQLRSQARTLITFAGMIPYRTSGDTNARLVQMEVLMN

SEQID No:202

MLLVLECVLF SVAQGYFRMDSSATQFHIETHENTSGLWSIWYRNHFDRSVVLNDVFLSK

ETKHMLKILNFTGPLFLPPGCWNIFSLKLAVKDIAINLFTNVFLT TNIGAIFAIP LQIYSAPTK  
 EGSLGFEVIAHCGMHYFMGKSKAGNPWNWNGSLSLDQSTWNVDSELANKLYERWKKY  
 KNGDVCKRNVLGTTTRFAHLKKSKESESFVFFLPRLIAEPGLMLNFSATALRSRMIKYFVV  
 QNPSSWPVSLQLLPLSLYPKPEALVHLLHRWFGTDMQMINFTTGEFQLTEACPYLGTH  
 SEESRFGILHLHLQPLEMKRVGVVFTPADYGKVTSLILIRNNLTVIDMIGVEGFGARELLK  
 VGGRLPGAGGSLRFKVPESTLMDCRRQLKDSKQILSITKNFKVENIGPLPITVSSLKINGY  
 NCQGYGFEVLDCHQFSLDPNTSRDISIVFTP DFTSSWVIRDL SLVTAADLEFRFTLNVTL  
 PHHLLPLCADVVPGPSWEESFWRLTVFFVSL SLLGVILIAFQQAQYILMEFMKTRQRQN  
 ASSSSQQNNGPMDVISPHSYKSNCKNFLDTYGPSDKGRGKNCLPVNTPQSRIQNAAK  
 RSPATYGHSQKKHKCSVYYSKHKTSTAAASSTSTTTEEKQTSPLGSSLPAAKEDICTDA  
 MRENWISLRYASGINVNLQKNLTLPKNLLNKEENTLKNTIVFSNPSSECSMKEGIQTCMF  
 PKETDIKTSSENTAEFKERELCPLKTSKKLPENHLPRNSPQYHQPDLP EISRKNNGNQQ  
 VPVKNEVDHCENLKKVDTKPSSEKKIHKTSREDMFSEKQDIPFVEQEDPYRKKKLQEKR  
 EGNLQNLNWSKSRTCRKNKKRGVAPVSRPPEQSDLKLVCSDFERSELSSDINVRSWCI  
 QESTREVCKADAEIASSLPAAQREAGYYQKPEKKCVDFKFCSDSSSDCGSSSGSVRAS  
 RGSWGSWSSTSSSDGDKKPMVDAQHFLPAGDSVSQNDFPSEAPISLNL SHNICNPMT  
 VNSLPQYAEPSCPSLPAGPTGVEEDKGLYSPGDLWPTPPVCVTSSLNCTLENGVPCVI  
 QESAPVHNSFIDWSATCEGQFSSAYCPELENDYNAFPEENMNYANGFPCPADVQTDFI  
 DHNSQSTWNTPPNMPAAWGHASFISSPPYLTSTRSLSPMSG LFGSIWAPQSDVYENC  
 CPINPTTEHSTHMENQAVVCKEYYPGFNPFRA YMNLDIWTTTANRNANFPLSRDSSYC  
 GNV

SEQID No:203

ASGEWRVSGGRPAGAGRPEEALAAGSDPRGAAARLACSAPTPGGGTMPFD FRRFDIY  
 RKVPKDLTQPTYTGAIISICCLFILFLFLSELTGFITTEVVNELYVDDPDKDSGGKIDVSL  
 NISLPNLHCELVGLDIQDEMGRHEVGHIDNSMKIPLNNGAGCRFEGQFSINKVPGNFHV  
 STHSATAQPQNPD MTHVIHKLSFGDTLQVQNIHGAFNALGGADRLTSNPLASHDYILKIV  
 PTVYEDKSGKQRYSYQYTVANKEYVAYSHTGRIIPAIWFRYDLSPITVKYTERRQPLYRF  
 ITTICAIIGGTFTVAGILDSCIFTASEAWKKIQLGKMH

SEQID No:204

NSKKMQSWYSMLSPTYKQRNEDFRKLFSKLPEAERLIVDYSCALQREILLQGRLYLSEN  
 WICFYSNIFRWETTISIQLKEVTCLKKEKTAKLIPNAIQICTESEKHFFTSFGARDRCFLIF  
 RLWQNALLEKTLSPRELWHLVHQC YGSELGLTSEDEDYVSPLQLNGLGTPKEVGDVIA

LSDITSSGAADRSQEPSPVGSRRGHVTPNLSRASSDADHGAEEDKEEQVDSQPDASS  
 SQTVTPVAEPPSTEPTQPDGPTTLGPLDLLPSEELLTDTSNSSSSTGEEADLAALLPDLS  
 GRLLINSVFHVGAERLQQMLFSDSPFLQGFLQQCKFTDVTLSPWSGDSKCHQRRVLT  
 TIPISNPLGPKSASVVETQTLFRRGPQAGGCVVDSEVLTQGIPYQDYFYTAHRYCILGLA  
 RNKARLRVSSEIRYRKQPWSLVKSLIEKNSWSGIEDYFHHLERELAKAEKLSLEEGGKD  
 ARGLLSGLRRRKRPPLSWRAHGDGPQHDPDP CARAGIHTSGSLSSRFSEPSVDQGGPG  
 AGIP SALVLISIVSLIILIALNVLLFYRLWSLERTAHTFESWHS LALAKGKFPQTATEWAEIL  
 ALQKQFHSVEVHKWRQILRASVELLDKMFSLKHLHQGITVSDPPFDTQPRPDDSF

SEQID No:205

MLGLLVALLALGLAVFALLDVWYLVRLPCAVLRARLLQPRVRDLLAEQRFPGRVLP  
 DLLLHMNNARYLREADFARVAHLTRCGVLGALRELRAHTVLAASCARHRRSLRLL  
 VRTRLLGWDDRAFYLEARFVSLRDGFVCALLRFRQHLLGTSPERVVQHLCQRRVE  
 PPPELPADLQHWISYNEASSQLLRMESGLSDVTKDQ

SEQID No:206

MTLARFVLALMLGALPEVVGFDVSLNDSLHSHRHSPAGPHYPPYLLPTQQRPPTTRP  
 PPPLPRFPRPPRALPAQRPHALQAGHTPRPHPWGCPAGEPWVSVTDFGAPCLRWA  
 EVPPFLERSPPASWAQLRGQRHNFCSRSPDGAGRPWCIFYGDARGKVDWGYCD  
 CRHGSVRLRGGKNEFEGTVEVYASGVWGTVCSSHWDDSDASVICHQLQLGGKGI  
 AKQTPFSGLGLIPIYWSNVRCRGDEENILLCEKDIWQGGVCPQKMAAAVTCSFS  
 HGPFTFPIIRLAGGS SVHEGRVELYHAGQWGTVCDDQWDDADAEVICRQLGLSG  
 IAKAWHQAYFGEGSGPV MLDEV RCTGNEL SIEQCPKSSWGEHNCGHKEDAGV  
 SCTPLTDGVIRLAGGKGSHEGR LEVYYRGQWGTVCDDGWTELNTYVVC  
 RQLGFKYKQASANHFEESTGPIWLDDVSCS GKETRFLQCSRRQWGRHDC  
 SHREDVSIACYPGGEGHRLSLGFPVRLMDGENKKEGR VEVFINGQWGTIC  
 DDGWTDKDAAVICRQLGYKGPARTMAYFGEGKGPIHVDNVKCT GNERSL  
 ADCIKQDIGRHNCRHSEDAGVICDYFGKKASGNSNKESSLSSVCGLRLLHRRQ  
 KRIIGGKNSLRGGWPWQVSLRLKSSHGDGRLLCGATLLSSCWVLTAAHCFK  
 RYGNSTR SYAVRVGDYHTLVPEEFEEEEIGVQQIVIHREYRPDRSDYDIAL  
 VRLQGPEEQCARFSSH VLPACLPLWRERPQKTASNCYITGWGDTGRAY  
 SRTLQQAAPLLPKRFCEERYKGRFT GRMLCAGNLHEHKRVDSCQGD  
 SGGPLMCERPGESWVVYGVTSWGYGCGVKDSPGV YTKVSAFVPWIKSVTKL



SEQID No:207

MEDGGLTAFEEDQRCLSQSLPLPVSAEGPAAQTTAEPSRSFSSAHRHLSRRNGLSRLC  
 QSRTALSEDRWSSYCLSSLAQNICTSKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSS  
 GWSSPLLPAVPCNPKNKAIFTVDAKTTEILVANDKACGLLGYSSQDLIGQKLTQFFLRSDS  
 DVVEALSEEHEADGHAADVFGTVVDIISRSGEKIPVSVWMKRMQRERRLCCVVVLEP  
 VERVSTWVAFQSDGTVTSCDSLFAHLHGYSVSGEDVAGQHITDLIPSVQLPPSGQHIPKN  
 LKIQRSVGRARDGTTFFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLP  
 DGTIHGINHSFALTFLGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNE  
 SGCGERTLDPWQQGDPAEGGQDPRINVVLGGHVPRDEIRKLMESQDIFTGTQTELI  
 AGGQLLSCLSPQPAPGVDNVPEGSLPVHGEQALPKDQQITALGREEPVAIESPGQDLL  
 GESRSEPVDVKPFASCEDSEAPVPAEDGGSDAGMCGLCQKAQLERMGVSGPSGSDL  
 WAGAAVAKPQAKGQLAGGSLLMHCPCYGSEWGLWWRSQDLAPSPSGMAGLSFGTP  
 TLDEPWLGVENREELQTCLIKEQLSQLSLAGALDVPHAELVPTECQAVTAPVSSCDLG  
 GRDLGGCTGSSSACYALATDLPGGLEAVEAQEVDVNSFSWNLKELFFSDQTDQTSS  
 NCSCATSELRETPSSLAVGSDPDVGSLEQEGSCVLDRELLLTGTCTVDLGQGRRFRE  
 SCVGHDPTEPLEVCLVSSEHYAASDRESPGHVPSTLDAGPEDTCPSAEEPRLNVQVTS  
 TPVIVMRGAAGLQREIQEGAYSGSCHHRDGLRLSIQFEVRRVELQGPTPLFCWLVDK  
 LLHSQRDSAARTRLFLASLPGSTHSTAAELTGPSLVEVLRARPWFEEPPKAVELEGLAA  
 CEGEYSQKYSTMSPLGSGAFGFVWTAVDKEKNKEVVVKFIKKEKVLEDCWIEDPKLGK  
 VTLEIAILSRVEHANIHKVLDIFENQGFFQLVMEKHGSGLDLFAFIDRHPRLDEPLASYIFR  
 QLVSAVGYLRLKDIIHRDIKDENVIAEDFTIKLIDFGSAAYLERGKLFYTFCTIEYCAPEV  
 LMGNPYRGPELEMWSLGVTLTYLVFEENPFCELEETVEAAIHPPYLVSKELMSLVSGLL  
 QPVPERRTTLEKLVTDPWVTQPVNLADYTWEEVCRVKNKPESGVLSAASLEMGNRSLS  
 DVAQAQELCGGPVPGAPNGQGCLHPGDPRLTS

SEQID No:208

MEPGTGGSRKRLGPRAGFRFWPPFFPRRSQAGSSKFPTPLGPENSGNPTLLSSAQPE  
 TRVSYWTKLLSQLLAPLPGLLQKVLWSQLFGGMFPTRWLDFAGVYSALRALKGREKP  
 APTAQKSLSSLQLDSSDPSVTSPLDWLEEGIHWQYSPPDLKLELKAKGSALDPAAQAF  
 LLEQQLWGVVELLPSSLQSRLYSNRELGSSPSGPLNIQRIDDFS VVS YLLNPSYLD CFPRL  
 EVSYQNSDGNSEVVGFTLTPESSCLREDHCHPQPLSAELIPASWQGCPLSTEGLPEI  
 HHLRMKRLEFLQQASKGQDLPTPDQDNGYHSLEEEHSLLRMDPKHCRDNPTQFVPAA  
 GDIPGNTQESTEEKIELLTTEVPLALEEESPSEGCPSSSEIPMEKEPGEGRISVVDYSYLE  
 GDLPISARPACSNKLIDYILGGASSDLETSSDPEGEDWDEEAEDDGFDSDSSLSDSDLE

QDPEGLHLWNSFCSDVPYNPQNFTATIQTAAARIVPEEPSDSEKDLSGKSDLENSSSQSG  
 SLPETPEHSSGEEDDWESSADEAESLKLWNSFCNSDDPYNPLNFKAPFQTSGENEKG  
 CRDSKTPSESIVAISECHTLLSCKVQLLGSQESECPDSVQRDVLGGRRHHTHVKKRVTF  
 LEEVTEYYISGDEDRKGPWEEFARDGCRFQKRIQETEDAIGYCLTFEHRERMFNRLQG  
 TCFKGLNVLKQC

SEQID No:209

MNLERSNEEKLNLCKRYLGGFAFLPFLWLVNIFWFFREAFVLPAYTEQSQIKGYVWR  
 SAVGFLFWVIVLTWITIFQIYRPRWGALGDYLSFTIPLGTP

SEQID No:210

MTELPAPLSYFQNAQMSEDNHLSTNDNRERQEHNDRRSLGHPEPLSNGRPQGNRSR  
 QVVEQDEEEDEELTLKYGAKHVIMLFVPVTLCMVVVVATIKSVSFYTRKDGQLIYTPFTE  
 DTETVGQRALHSILNAAIMISVIVVMTILLVVLKYRCYKVIHAWLISSLLLLFFFSFIYLGE  
 VFKTYNVAVDYITVALLIWNLGVVGMISIHGKPLRLQQAYLIMISALMALVFIKYLPEWT  
 AWLILAVISVYDLVAVLCPKGPLRMLVETAQERNETLFPALIYSSTMVWLVNMAEGDPEA  
 QRRVSKNSKYNNAESTERESQDTVAENDDDGGFSEWEAQRDHSHLGPHERSTPESRAAV  
 QELSSSILAGEDPEERGVKLGLGDFIFYSVLVGKASATASGDWNTTIACFVAILIGLCLTL  
 LLLAIFKKALPALPISITFGLVFYFATDYLVPFMDQLAFHQFYI

SEQID No:211

MAAETLLSSLLGLLLLGLLLPASTGGVGSNLLEELSEMRYGIEILPLPVMGGQSQSSDV  
 VIVSSKYKQRYECRLPAGAIHFQREREEETPAYQGPGIPELLSPMRDAPCLLTKTDWWT  
 YEFYGRHIQQYHMEDSEIKGEVLYLGYYSQAFDWDDDETAKASKQHRLKRYHSQTYG  
 NGSKCDLNGRPREAEVRFLCDEGAGISGDYIDRVDEPLSCSYVLTIRTPRLCPHPLLRP  
 PPSAAPQAILCHPSLQPEEYMAVYVQRQADSKQYGDKIIEELQDLGPQVWSETKSGVAP  
 QKMAGASPTKDDSKDSDFWKMLNEPEDQAPGGEEVPAEEQDPSPEAADSASGAPND  
 FQNNVQVKVIRSPADLIRFIEELKGGTKKGKPNIGQECPVDDAAEVPQREPEKERGDPE  
 RQREMEEEEEDEDEDEDEDEDERQLLGEFEKELEGILLPSDRDRLRSEVKAGMERELN  
 IIQETEKELDPDGLKKESERDRAMLALTSTLNKLIKRLKQSPPELVKKHKKKRVVPKKP  
 PPSPQPTTEEDPEHRVRVRVTKLRLGGPNQDLTVLEMKRENPLKQIEGLVKELLEREG  
 LTAAGKIEIKIVRPWAEGTEEGARWLTDTRNLKEIFFNILVPGAEAAQKERQRQKELE  
 SNYRRVWGSPGGEGTGDLDEFDF

SEQID No:212

MAVVPLLLLGGGLWSAVGASSLGVVTCGSVVKLLNTRHNVRLHSHDVRVGSGSGQQSV  
 TGVTSVDDSNYSYWRIRGKSATVCERGTPIKCGQPIRLTHVNTGRNLHSHHFTSPLSGN  
 QEVSAFGEEGEGDYLDDWTVLCNGPYWVRDGEVRFKHSSTEVLSSVTGEQYGRPISG  
 QKEVHGMAQPSQNNYWKAMEGIFMKPSELLKAEAHHAEL

SEQID No:213

MEASGKLICRQRQVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQRE  
 FSRRGVRVVSRRGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLRQVLLESPFEFF  
 QAELQVIDINDHSPVFLDKQMLVKVSESSPPGTAFPLKNAEDLDIGQNNIENYIISPNSYF  
 RVLTRKRSDGRKYPELVLDNALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVVDVND  
 NAPEFQQPFYRVQISEDSPISFLVVKVSATDVDVTGVNGEISYSLFQASDEISKTFKVDFLT  
 GEIRLKKQLDFEKFQSYEVNIEARDAGGFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPE  
 NAPETVVALFSVSDLDSENGKISCSIQEDLPFLKSSVGNFYTLTETPLDRESRAEYN  
 VTITVTDLGTPRLTTHLNMTVLVSDVNDNAPAFQTQSYTLFVRENNSPALHIGSVSATDR  
 DSGTNAQVTYSLLPPQDPHLPLASLVSINTDNGHLFALRSLDYEALQAFEFVRVGASDRG  
 SPALSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDS  
 GQNAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPCS  
 ATATLHLLLVDGFSQPYPPLPEAAPAQGQADSLTVYLVVALASVSSLFLFSVLLFVAVLLC  
 RRSRAASVGRCSVPEGPFGHLVDVRGTGSLSQNYQYEVCLAGGSGTNEFQFLKPVL  
 PNIQGHSGFPEMEQNSNFRNGFGFSLQLK

SEQID No:214

MASRGVVGIFFLSAVPLVCLELRRGIPDIGIKDFLLLCGRILLALLTLISVTTSWLNSFKS  
 PQVYLKEEEEKNEKRQKLVRKKQQEAQGEKASRYIENVLKPHQEMKLRKLEERFYQMT  
 GEAWKLSSGHKLGGDEGTSQTSFETSNREAAKSQNLPKPLTEFPSPAEQPTCKEIPDL  
 PEEPSQTAEVVTVALRCPSGNVLRRLRFLKSYSSQVLFDWMTRIGYHISLYSLSTSFP  
 RPLAVEGGQSLEDIGITVDTVLILEEKEQTN

SEQID No:215

MAAAEEEDGGPEGPNRERGGAGATFECNICLETAREAVVSVCGLHLYCWPCLHQWLET  
 RPERQECPVCKAGISREKVVPLYGRGSQKPQDPRLKTPPRPQGQRPAPESRGGGFQPF  
 GDTGGFHFSFGVGAFPGFFTTVFNAHEPFRRGTGVDLGQGHPASSWQDSLFLFLAIF  
 FFFWLLSI

SEQID No:216

MKFLLDILLLLPLLIVCSLESFVKLFIPKRRKSVTGEIVLITGAGHGIGRLTAYEFAKLKSKL  
VLWDINKHGLEETAACKCKGLGAKVHTFVVDCSNREDIYSSAKKVKAEIGDVSILVNNAGV  
VYTSDLFATQDPQIEKTFEVNVLAHFWTTKAFLPAMTKNNHGHIVTVASAAGHVSVPFLL  
AYCSSKFAAVGFHKTLTDELAALQITGVKTTCLCPNFVNTGFIKNPSTSLGPTLEPEEVV  
NRLMHGILTEQKMIFIPSSIAFLTTLERILPERFLAVLKRKISVKFDAVIGYKMKAQ

SEQID No:217

MWSAGRGGAAWPVLLGLLLALLVPGGGAAKTGAELVTCGSVLKLLNTHHRVRLHSHDI  
KYGSGSGQQSVTGVEASDDANSYWRIRGGSEGCGPCGSPVRCGQAVRLTHVLTGKN  
LHTHHFPSPLSNNQEVSAFGEDGEEDDLWTVRCSGQHWEREAAVRLQHVGTSVFL  
SVTGEQYGSPIRGQHEVHGMPSANTHNTWKAMEGIFIKPSVEPSAGHDEL

SEQID No:218

GRWASGEMAPSGSLAVPLAVLVLLLWGAPWTHGRRSNVRVITDENWRELLEGDWMIE  
FYAPWCPACQNLQPEWESFAEWGEDLEVNIKVDVTEQPGLSGRFIITALPTIYHCKDG  
EFRRYQGPRTKKDFINFISDKEWKSIEPVSSWFGPGSVLMSSMSALFQLSMWIRTCHN  
YFIEDLGLPVWGSYTVFALATLFSGLLLGLCMIFVADCLCPSKRRRRPQPYPYPSKKLLSE  
SAQPLKKVEEEEQEADEEDVSEEEAESKEGTNKDFPQNAIRQRSLSLGPLATDKS

SEQID No:219

HPAGLAAAAAGTPRLPSKRRIPVSQPGMADPHQLFDDTSSAQSRGYGAQRAPGGLSY  
PAASPTPHAAFLADPVSNMAMAYGSSLAAQGKELVDKNIDRFIPITKLKYYFAVDTMYV  
GRKLGLLFFPYLHQDWEVQYQQDTPVAPRFDVNAPDLYIPAMAFITYVLVAGLALGTQD  
RFSPDLLGLQASSALAWLTLEVLAILLSLYLVTVNTDLTTIDLVAFLGYKYVGMIGGVLMG  
LLFGKIGYYLVLGWCCVAIFVFMIRTLRLKILADAAAEGVPVRGARNQLRMYLTMAVAAA  
QPMLMYWLTFHLVR

SEQID No:220

MAATALLEAGLARVLFYPTLLYTLFRGKVPGRAHRDWYHRIDPTVLLGALPLRSLTRQLV  
QDENVRGVITMNEEYETRFLCNSSQEWKRLGVEQLRLSTVDMTGIPTLDNLQKGVQFA  
LKYQSLGQCVYVHCKAGRSRSATMVAAYLIQVHKWSPEEAVRAIAKIRSYIHIRPGQLDV  
LKEFHKQITARATKDGTFFVSKT



SEQID No:221

MNTVLSRANSLFAFSLSVMAALTFGCFITTA FKDRSVPVRLHVSRI MLKNVEDFTGPRER  
 SDLGFITSDITADLENIFDWNVKQLFLYLSAEYSTKNNALNQVVLWDKIVLRGDNPKLLLK  
 DMKTKYFFFDDGNGLKGNRNVTLTLSWNVVPNAGILPLVTGSGHVSVPFPD TYEITKSY

SEQID No:222

MALRGFCSADGSDPLWDWNVTWNTSNPDFTKCFQNTVLVWVPCFYLWACFPFYFLYL  
 SRHDRGYIQMTPLNKTKTALGFLWIVCWADLFYSFWERSRGIFLAPVFLVSPTLLGITT  
 LLATFLIQLERRKGVQSSGIMLTFWLVALVCALAILRSKIMTALKEDAQVDLFRDITFYVYF  
 SLLLIQLVLSCFSDRSPLFSETIHDPNPCPESSASFLSRITFWWITGLIVRGYRQPLEGSD  
 LWSLNKEDTSEQVVPVLVKNWKKECAKTRKQPVKVYSSKDPAPKESKVDANEEV  
 EALIVKSPQKEWNPSLFKVLYKTFGPYFLMSFFFKAIHDLMMFSGPQILKLLIKFVNDTKA  
 PDWQGYFYTVLLFVTACLQTLVLHQYFHICFVSGMRIKTAVIGAVYRKALVITNSARKSS  
 TVGEIVNLMSVDAQRFMDLATYINMIWSAPLQVILALYLLWNLGPSVLGAVAVMVL MVP  
 VNAVMMAMKTKTYQVAHMKSKDNRIKLMNEILNGIKVLKLYAWELAFKDKVLAIRQEELKV  
 LKKSAYLSAVGTFTWVCTPFLVALCTFAVYVTIDENNILDAQTAFVSLALFNILRFPLNILP  
 MVISSIVQASVSLKRLRIFLSHEELEPDSIERRPVKDGGGTNSITVRNATFTWARSDPPTL  
 NGITFSIPEGALVAVVGQVGCGKSSLLSALLAEMDKVEGHVAIKGVNLSGGQKQRVSLA  
 RAVYSNADIYLFDDPLSAVDAHVGKHIFENVIGPKGMLKNKTRILVTHSMSYLPQVDVIIV  
 MSGGKISEMGSYQELLARDGAFAEFLRTYASTEQE QDAEENGVTGVSGPGKEAKQME  
 NGMLVTDSAGKQLQRQLSSSSSSYSGDISRHHNSTAELQKAEAKKEETWKLMEADKAQ  
 TGQVKLSVYWDYMKAI GLFISFLSIFLFCNHVSALASNYWLSLWTDDPIVNGTQEHTK  
 VRLSVYGALGISQGI AVFGYSMAVSIGGILASRCLHVDLLHSILRSPMSFFERTPSGNLVN  
 RFSKELDTVDSMIPEVIKMFMSGSLFN VIGACIVILLATPIAAIIIPPLGLIYFFVQRFYVASSR  
 QLKRLSVSRSPVYSHFNETLLGVSVIRAFEEQERFIHQSDLKVDENQKAYYPSIVANR  
 WLAVRLECVGNCIVLFAALFAVISRHSLSAGLVGLSVSYSLQVTTYLNWLVRMSSEMET  
 NIVAVERLKEYSETEKEAPWQIQETAPPSSWPQVGRVEFRNYCLRYREDLDFVLRHINV  
 TINGGEKVGIVGRTGAGKSSLTLGLFRINESAEGEI IIDGINIAKIGLHDLRFKITIIPQDPVLF  
 SGSLRMNLDPF SQYSDEEVWTSLELAHLKDFVSALPKLDHECAEGGENLSVGQRQLV  
 CLARALLRKT KILVLDEATAAVDLETDDLIQSTIRTQFEDCTVLTIAHRLNTIMDYTRVIVLD  
 KGEIQEYGAPSDLLQQRGLFY SMAKDAGLV

SEQID No:223

MARGKAKEEGSWKKFIWNSEKKEFLGRTGGSWFKILLFYVIFYGCLAGIFIGTIQVMLLTI  
SEFKPTYQDRVAPPGLTQIPQIQKTEISFRPNPKSYEAYVLNIVRFLEKYKDSAQRDDM  
IFEDCGDVPSEPKERGDFNHERGERKVCRFKLEWLGNC SGLNDETYGYKEGKPCIIKL  
NRVLGFKPKPPKNESLETYPVMKYNPVLPVQCTGKRDEDKDKVGNVEYFGLGNSPG  
FPLQYYPPYYGKLLQPKYLQPLLAVQFTNLTMDTEIRIECKAYGENIGYSEKDRFQGRFDV  
KIEVKS

SEQID No:224

MKVARFQKIPNGENETMIPVLTSKKASELPVSEVASILQADLQNGLNKCEVSHRRAFHG  
WNKFDISEDEPLWKKYISQFKNPLIMLLLASAVISVLMHQFDDAVSITVAILIVVTVAFVQE  
YRSEKSLEELSKLVPPECHCVREGKLEHTLARDLVPGDTVCLSVGDRVPADLRLFEAVD  
LSIDESSLTGETTPCSKVTAPQPAATNGDLASRSNIAFMGTLVRCGKAKGVVIGTGENS  
EFGGEVFKMMQAE EAPKTPLQKSMDLLGKQLSFYSFGIIGIIMLVGWLLGKDILEMFTISVS  
LAVAAIPEGLPIVVTVTALGVMMRMVKKRAIVKKLPIVETLGCCNVICSDKTGTLTKNEMT  
VTHIFTSDGLHAEVTGVGYNQFGEVIVDGDVHGFYNPAVSRIVEAGCVCNDAVIRNNT  
LMGKPTEGALIALAMKMGLDGLQQDYIRKAEYPFSSEQKWMMAVKCVHRTQQDRPEICF  
MKGAYEQVIKYCTTYQSKGQTLTLTQQQRDVYQQEKARMGSAGLRVLALASGPELGQ  
LTFLGLVGIIDPPRTGVKEAVTTLIASGVSIKMITGDSQETAVAIASRLGLYSKTSQSVSGE  
EIDAMDVQQLSQIVPKVAVFYRASPRHKMKIIKSLQKNGSVVAMTGDGVNDAVALKAAD  
IGVAMGQTGTDVCKEAADMILVDDDFQTIMSAIEEGKGIYNNIKNFVRFQLSTSI AALT LIS  
LATLMNFPNPLNAMQILWINIIMDGPPAQSLGVEPVDKDVIRKPPRNWKDSILTKNLILKIL  
VSSIIIVCGTLFVFWREL RDNVITPRDTTMTFTCFVFFDMFNALSSRSQTKSVFEIGLCSN  
RMFCYAVLGSIMGQLLVIYFPPLQKV FQTESLSILDLLFLLGLTSSVCIVAEI IKKVERSRE  
KIQKHVSSTSSSFLEV

SEQID No:225

MAKNRRDRNSWGGFSEKTYEWSSEEEEPVKKAGPVQVLIVKDDHSFELDETALNRILL  
SEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVG DYNEPLTGFSWRG  
GSERETTGIQIWSEIFLINKPDGKKVAVLLMDTQGT FDSQSTLRDSATVFALSTMISSIQV  
YNLSQNVQEDDLQHLQLFTEYGR LAMEETFLKPFQSLIFLVRDWSFPYEF SYGADGGA  
KFLEKRLKVSGNQHEELQNVRKHIHSCFTNISCFLPHPG LKVATNP NFDGKLKEIDDEFI  
KNLKILIPWLLSPESLDIKEINGNKITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANN  
LAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTKHLQLKEESVKLFRGVKKMGGE EFS

RRYLQQLESEIDELIYIQYIKHNDSKNIFHAARTPATLFVVIFITYVIAGVTGFIGLDIIASLCN  
MIMGLTLITLCTWAYIRYSGEYRELGAVIDQVAAALWDQGSTNEALYKLYSAAATHRHLY  
HQAFTPKESESTEQSEKKKM

SEQID No:226

MGCCSSASSAAQSSKREWKPLEDRSCTDIPWLLLFI LFCIGMGFICGFSIATGAAARLVS  
GYDSYGNICGQKNTKLEAIPNSGMDHTQRKYVFFLDPCNLDLINRKIKSVALCVAACPR  
QELKTLSDVQKFAEINGSALCSYNLKPSEYTTSPKSSVLC PKLPVPASAPIPFFHRCAPV  
NISCYAKFAEALITFVSDNSVLHRLISGVM TSKEIILGLCLLSVL SMILMVIIRYISRVLVWIL  
TILVILGSLGGTGVLWWLYAKQRRSPKETVTPEQLQIAEDNLRALLIY AISATVFTVILFLIM  
LVMRKRVALTIALFHVAGKVFIHLPLL VFQPFWTFFALVLFWVYWIMTLLFLGTTGSPVQ  
NEQGFVEFKISGPLQYMWVYHVVG LIWISFILACQQMTVAGAVVTYYFTRDKRNL PFT  
PILASVNRLIRYHLGTVAKGSFIITLVKIPRMILMYIHSQ LKGKENACARCVLKSCICCLWC  
LEKCLNYLNQ NAYTATAINSTNFCTSAKDAFVILVENALRVATINTVGDFMLFLGKVLIVC  
STGLAGIMLLNYQQDYTVWVLPLIIVCLFAFLVAHCFLSIYEMVVDV LFLCFAIDTKYNDG  
SPGREFYMDKVLMEFVENS RKAMKEAGKGGVADSRELKPMLKKR

SEQID No:227

EKSGGPGTREREREKREERQSAWGRKERGREGWVRRRRERSAANPRRRRAWSPSQNS  
SPSRSRSQGGGCRDRQPCMMHLRLFCILLA AVSGAEGWGYYGCDEELVGPLYARSLG  
ASSYYSLLTAPRFARLHGISGWSPRIGDPNPWLQIDLMKKHRIRAVATQGSFNSWDWV  
TRYMLLYGDRVDSWTPFYQRGHNSTFFGNVNESAVVRHDLHFHFTARYIRIVPLAWNP  
RGKIGLRLGLYGCPYKADILYFDGDDAISYRFPRGVS RSLWDVFAFSFKTEEKDGLLLHA  
EGAQGDYVTLELEGAHLLLHMSLGSSPIQPRPGHTTVSAGGVLNDQHW HYVRVDRFG  
RDVNFTLDGYVQRFILNGDFERLNLDTEMFIGGLVGAARKNLAYRHNFRGCIENVIFNRV  
NIADLAVRRHSRITFEGKVAFRCLDPVPHPI NFGGPHNFVQVPGFPRRGRLAVSFRFRT  
WDLTGLLLFSRLGDGLGHVELT LSEGQVNV SIAQSGRKKLQFAAGYRLNDGFWHEVNF  
VAQENHAVISIDDVEGAEVRVSYPLLIRTGTSYFFGGCPKPASRWDCHSNQTAFHGCM  
ELLKVDGQLVNLT LVEGRRLGFYAEVLFDTCGITDR CSPNMCEHDGRCYQSWDDFICY  
CELTGYKGETCHTPLYKESCEAYRLSGKTSGNFTIDPDGSGPLKPFVVYCDIRENRAWT  
VVRHDRLWTTRVTGSSMERPF LGAIQYWNASWEEVSALANASQHCEQWIEFSCYNSR  
LLNTAGGY PYSFWIGRNEEQHFYWGGSQPGIQR CACGLDRSCVDPALYCNC DADQPQ  
WRTDKGLLTFVDHLPVTQVVIGDTNRSTSEA QFFLRPLRCYGDRNSWNTISFHTGAALR  
FPPIRANHSLDVSFYFRTSAPSGVFLENMGGPYCQWRRPYVRVELNTSRDVVFAFDVG

NGDENLTVHSDDFEFNDDEWHLVRAEINVKQARLRVDHRPWVLRPMPPLQTYIWMEYD  
 QPLYVGSAELKRRPFVVGCLRAMRLNGVTLNLEGRANASEGTSPNCTGHCAHPRLPCF  
 HGGRCVERYSSYYTCDCLTAFDGPYCNHDIGGFFEPGTWMRYNLQSALRSAAREFSH  
 MLSRPVPGYEPGYIPGYDTPGYVPGYHGPYRLPDYPRPGRPVPGYRGPVYNVTGEE  
 VSFSFSTSSAPAVLLYVSSFVRDYMALIKDDGTLQLRYQLGTSPYVYQLTTRPVTDGQ  
 PHSINITRVYRNLFIQVDYFPLTEQKFSLLDVDSQLDSPKALYLGRVMETGVIDPEIQRYNT  
 PGFSGCLSGVRFNNVAPLKTHFRTPRPMATAELAEALRVQGELSESNCGAMPRLVSEVP  
 PELDPWYLPPDFPYHDEGWVAILLGFLVAFLLLGLVGMLVLFYLQNHRYKGSYHTNEP  
 KAAHEYHPGSKPPLPTSGPAQVPTPTAAPNQAPASAPAPAPTAPAPGPRDQNLQPIL  
 EESRSE

SEQID No:228

MGNRGMEDLIPLVNRLQDAFSAIGQNADLDLPQIAVVGGQSAGKSSVLENFVGRDFLP  
 RGSGIVTRRPLVLQLVNATTEYAEFLHCKGKKFTDFEEVRLEIEAETDRVTGTNKGISPV  
 PINLRVYSPHVLNLTLDLPGMTKVPVGDQPPDIEFQIRDMLMQFVTKENCLILAVSPAN  
 SDLANSALKVAKEVDPQGQRTIGVITKLDLMDEGTDARDVLENKLLPLRRGYIGVVNR  
 SQKDIDGKKDITAALAAERKFFLSHPSYRHLADRMGTPYLQKVLNQQLTNHIRDITLPLGLR  
 NKLQSQLLSIEKEVEEYKNFRPDDPARKTKALLQM VQQFAVD FEKRIEGSGDQIDTYEL  
 SGGARINRIFHERFPFELVKMEFDEKELRREISYAIKNIHGIRTGLFTPDMAFETIVKKQVK  
 KIREPCLKCVDMMVISELISTVRQCTKKLQQYPRLREEMERIVTTHIREREREGRRTKEQVMLLI  
 DIELAYMNTNHEDFIGFANAQQRSNQMNNKKKTSGNQDEILVIRKGWLTINNIGIMKGGSK  
 EYWFVLTAENLSWYKDDEEKEKKYMLSVDNLKLRDVEKGFMSKHFALFNTEQRNVY  
 KDYRQLELACETQEEVDSWKASFLRAGVYPERVGDKEKASETEENGSDSFMHSM DPQ  
 LERQVETIRNLVDSYMAIVNKTVRDLMPKTIMHLMINNTKEFIFSELLANLYSCGDQNTLM  
 EESAEQAQRRDEMLRMYHALKEALSIIGNINTTTVSTPMPPPVD DS WLQVQSV PAGRR  
 SPTSSPTPQRRAPAVPPARPGSRGPAPGPPPAGSALGGAPPVPSRPGASPD PF GPPP  
 QVPSRPNRAPPGVPSRSGQASPSRPESPRPPFDL

SEQID No:229

MAARRQGPARSANPRPQFPGVCGREHAATLRAPGRGGGGASPAQIGTRGRGGHNFAP  
 NLTARSAVTSGLGPPAAVMVGSLNCIVAVSQNMGIGKNGDLPWPPLRNEFRYFQRM  
 TTTSSVEGKQNLVIMGKKTWFSIPEKNRPLKGRINLVLSRELKEPPQGAHFLSRSLDDAL  
 KLTEQPELANKVDMVWIVGGSSVYKEAMNHPGHLKLFVTRIMQDFESDTFFPEIDLEKY  
 KLLPEYPGVLSDVQEEKGIKYKFEVYEKND



SEQID No:230

MDRGTLPLAVALLASCSLSPTSLAETVHCDLQPVGPERGEVTYTTTSQVSKGCVAQAP  
 NAILEVHVLFLFPTGPSQLELTQASKQNGTWPREVLLVLSVNSSVFLHLQALGIPLHL  
 AYNSSLVTFQEPPGVNTTELPSFPKTQILEWAAERGPITSAAELNDPQSILLRLGQAQGS  
 LSFCMLEASQDMGRTLEWRPRTPALVRGCHLEGVAGHKEAHILRVLPGHSAGPRTVTV  
 KVELSCAPGDLDVILQGGPPYVSWLIDANHNMQIWTTGEYSFKIFPEKNIRGFKLPDTP  
 QGLLGEARMNLNASIVASFVELPLASIVSLHASSCGGRLQTSPAPIQTTPPKDTCSPELLM  
 SLIQTKCADDAMTLVLKKELVAHLKCTITGLTFWDPSCEAEDRGDKFVLRSAVSSCGMQ  
 VSASMISNEAVVNILSSSSPQRKKVHCLNMDLSLQGLYLSPHFLQASNTIEPGQQSF  
 VQVRVSPSVSEFLLQLDSCHLDLGPEGGTVELIQGRAAKGNCVSLSPSPEGDPFRFSFL  
 LHFYTVPIPKTGTLSTVALRPKTGSQDQEVHRTVFMRLNIISPDLSGCTSKGLVLPVAVL  
 GITFGAFLIGALLTAALWYIYSHTRSPSKREPVVAVAAPASSESSSTNHSIGSTQSTPCST  
 SSMA

SEQID No:231

MCASVKYNIRGPALIPRMKTKHRIYYITLFSIVLLGLIATGMFQFWPHSIESSNDWNVEKR  
 SIRDVPVVRLLPADSPIPERGDLSCRMHTCFDVYRCGFNPKNKIKVYIYALKKYVDDFGVS  
 VSNTISREYNELLMAISDSYYTDDINRACLFVPSIDVLNQNTLRIKETAAQAMAQLSRWD  
 RGTNHLLFNMLPGGPPDYNTALDVPRDRALLAGGGFSTWYRQGYDVSIPVYSPLSAE  
 VDLPEKGPGRQYFLLSSQVGLHPEYREDLEALQVKHGESVLVLDKCTNLSEGVLSVR  
 KRCHKHQVFDYPQVLQEATFCVVLRGARLGQAVLSDVLQAGCVPVVIADSYILPFSEVL  
 DWKRASVVVPEEKMSDVYSILQSIPQRQIEEMQRQARWFWWEAYFQSIKAIATLQIIND  
 RIYPYAAISYEEWNDPPAVKWGSVSNPLFLPLIPPQSQGFTAIVLTYDRVESLFRVITEVS  
 KVPSLSKLLVWNNQNKNPPEDSLWPKIRVPLKVVRTAENKLSNRFFPYDEIETEAVLAI  
 DDDIIMLTSDDELQFGYEVWREFPDRLVGYPGRHLWDHEMNKWKEYESEWTNEVSMVL  
 TGAIFYHKYFNYLYTYKMPGDIKNWVDAHMNCEDIAMNFLVANVTGKAVIKVTPRKKFK  
 CPECTAIDGLSLDQTHMVERSEKINKFASVFGTMPLKVVEHRADPVLYKDDFPEKLKSF  
 PNIGSL

SEQID No:232

MTGYTMLRNGGAGNGGQTCMLRWSNRIRLTWLSFTLFFVILVFFPLIAHYLTTLDEADE  
 AGKRIFGPRVGNELCEVKHVLDLCRIRESVSEELLQLEAKRQELNSEIAKLNKIEACKKS  
 IENAKQDLLQLKNVISQTEHSYKELMAQNQPKLSLPIRLLPEKDDAGLPPP KATRGCRLH

NCFDYSRCPLTSGFPVYVYDSDQFVFGSYLDPLVKQAFQATARANVYVTENADIACLYV  
 ILVGEMQEPVVLRPAAELEKQLYSLPHWRTDGHNHVIINLSRKSDTQNLLYNVSTGRAMV  
 AQSTFYTVQYRPGFDLVVSPLVHAMSEPNFMEIPPQVPVKRKYLFTFQGEEKIESLRSSL  
 QEARSFEEEMEGDPPADYDDRIIATLKAVQDSKLDQVLVEFTCKNQPKPSLPTEWALC  
 GEREDRLELLKLSTFALIITPGDPRLVISSGCATRLFEALEVGAVPVVLGEQVQLPYQDM  
 LQWNEAALVVPKPRVTEVHFLLRSLSDSDLLAMRRQGRFLWETYFSTADSIFNTVLAMI  
 RTRIQIPAAPIREEAAAEIPHRSGKAAGTDPNMADNGDLDLGPVETEPPYASPRYLRNFT  
 LTVTDFYRSWNCAPGPFHLFPHTPFDPVLPSEAKFLGSGTGFRPIGGGAGGSGKEFQA  
 ALGGNVPREQFTVVMLTYEREEVLMNSLERLNGLPYLNKVVVVWNSPKLPSEDLLWPD  
 IGVPIMVVRTEKNSLNNRFLPWNEIETEAILSIDDDAHLRHDEIMFGFRVWREARDRIVGF  
 PGRYHAWDIPHQSWLYNSNYSCELSMVLTGAFFHKYYAYLYSYVMPQAIRDMVDEYI  
 NCEDIAMNFLVSHITRKPPIKVTSRWTFRCPGCPQALSHDDSHFHERHKCINFFVKVYG  
 YMPLLYTQFRVDSVLFKTRLPHDKTKCFKFI

SEQID No:233

MGPGRPAPAPWPRHLLRCVLLLGCLHLGRPGAPGDAALPEPNVFLIFSHGLQGQCLEAQ  
 GGQVRVTPACNTSLPAQRWKWVSRNRLFNLTGMQCLGTGWPGTNTTASLGMYECDR  
 EALNLRWHCRTLGDQLSLLGARTSNISKPGTLERGDQTRSGQWRIYGSEEDLCALPY  
 HEVYTIQGNSHGKPCPTIPFKYDNQWFHGTCTSTGREDGHLWCATTQDYGKDERWGFC  
 PIKSNDCETFWDKDQLTDSCYQFNQSTLSWREAWASCEQQGADLLSITEIHEQTYING  
 LLTGYSSTLWIGLNDLDTSGGWQWSDNSPLKYLNWESDQPDNPSEENCGVIRTESSG  
 GWQNRDCSIALPYVCKKKPNATAEPTPPDRWANVKVECEPSWQPFQGH CYRLQAEK  
 RSWQESKKACLRGGGDLVSIHSMAELEFITKQIKQEVEELWIGLNDLKLQMNFEWSDG  
 SLVSFTHWHHPFEPNNFRDSLED CVTIWGPEGRWNDSPCNQSLPSICKKAGQLSQGAA  
 EEDHGCRCRGWTWHSPSCYWLGEDQVTYSEARRLCTDHGSQLVTITNRFEQAFVSSLI  
 YNWEGEYFWTALQDLNSTGSFFWLSGDEV MYTHWN RDQPGYSRGGCVALATGSAM  
 GLWEVKNCTSF RARYICRQSLGTPVTPELPGPDPTPSLTGSCPQG WASDTKLRYCYKV  
 FSSERLQDKKSWVQAQGACQELGAQLLSLASYEEEEHFVANMLNKIFGESEPEIHEQHW  
 FWIGLNR RDPRGGQSWRWSDGVGFSYHNFD RSRHDDDDIRGCAVLDLASLQWVAMQ  
 CDTQLDWICKIPRGTDVREPDDSPQGRREWLRFQEA EYKFFEHHSTWAQAQRIC TW F  
 QAELTSVHSQAELDFLSHNLQKFSRAQEQHWWIGLHTSESDGRFRWTDGSIINFISWA  
 PGKPRPVGKDKKCVYMTASREDWGDQRCLTALPYICKRSNVTKETQPPDLPTTALGG  
 CPSDWIQFLNKC FQVQGGQEPQSRVKWSEAQFSCEQQEAQLVTITNPLEQAFITASLPN  
 VTFDLWIGLHASQRDFQWVEQEPLMYANWAPGEPSPGSPAPSGNKPTSCAVVLHSPS

AHFTGRWDDRSCTEETHGFICQKGTDPSSLSPSPAALPPAPGTELSYLNNGTFRLLQKPLR  
 WHDALLCESHNASLAYVPDPYTQAFLTQAARGLRTPLWIGLAGEEGSRRYSWVSEEP  
 LNYVGWQDGEPPQQPGGCTYVDVDGAWRTTSCDTKLQGAVCGVSSGPPPPRRISYHG  
 SCPQGLADSAWIPFREHCYSFHMELLGHKEARQRCQRAGGAVLSILDEMENVFVWE  
 HLQSYEGQSRGAWLGMNFNPKGGTLVWQDNTAVNYSNWGPPGLGPSMLSHNSCYW  
 IQSNSGLWRPGACTNITMGVVCKLPRAEQSSFSPSALPENPAALVVVLMVLLLLALLTA  
 ALILYRRRRQSIERGAFEGARYSRSSSSPTEATEKNILVSDMEMNEQQE

SEQID No:234

MEDHQBHPIDIQTSKLLDWLVDRRHCSLKWQSLVLTIREKINAAIQDMPESSEEIAQLLSG  
 SYIHYFHCLRILDLLKGTEASTKNIFGRYSSQRMKDWQEIIALYEKDNTYLVELSSLLVRN  
 VNYEIPSLKKQIAKCCQLQQEYSRKEEEECQAGAAEMREQFYHSCKQYGITGENVRGEL  
 LALVKDLPSQLAEIGAAAQQLGEAIDVYQASVGFVCESPTEQVLPMLRFVQKRGNSTV  
 YEWRTGTEPSVVERPHLEELPEQVAEDAIDWGDGVEAVSEGTDSGISAEAAGIDWGI  
 FPESDSKDPGGDGIDWGDDAVALQITVLEAGTQAPEGVARGPDALTLEYTETRNOFL  
 DELMELEIFLAQRAVELSEEADVLSVSQFQLAPAILQQGTKEKMVTMVSVLEDLIGKLT  
 LQLQHLMILASPRYVDRVTEFLQQKLKQSLLALKKELMVQKQQEALEEQAALPKLD  
 LLEKTKELQKLEADISKRYSGRPVNLMTSL

SEQID No:235

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPHCHCEPDGRMLLRVDCSDLGLS  
 ELPSNLSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFGLYSLKVL  
 MLQNNQLRHVPTEALQNLRSLSRLDANHISYVPPSCFSGLSLRHLWLDDNALTEIP  
 VQAFRSLALQAMTLALNKHHPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLET  
 LDNLNNLDEFPTAIRTLNLKELGFHSNNIRSIPEKAFVGNPSLITIHFYDNPIQFVGRSA  
 FQHLPELRTLTLNGASQITEFPDLTGANLESLTLTGAQISSLPQTVCNQLPNLQVLDLSY  
 NLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLSLRSLNLAWNKAIIHPNAFSTLPS  
 LIKLDLSSNLLSSFPITGLHGLTHLKLGTGNHALQSLISSENFPELKVIEMPYAYQCCAFGV  
 CENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLDFFEDLKALHSVQC  
 SPSPGPFKPCHEHLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYISPIKLLIGVIAAVN  
 MLTGVSASVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLTLAALER  
 GFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEPTM  
 GYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCCSMVKHIALLLFTNCILNCPVAF

LSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVSLRKQTYVWTRSKHP  
SLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSPAYPVTESCHLSSVAFVPCL

SEQID No:236

MIASHLLAYFFTELNHDQVQKVDQYLYHMRLSDETLLEISKRFRKEMEKGLGATTHPTA  
AVKMLPTFVRSTPDGTEHGEFLALDLGGTNFRVLWVKVTDNGLQKVEMENQIYAIPEDI  
MRGSGTQLFDHIAECLANFMDKLQIKDKKLPLGFTFSFPCHQTKLDESFLVSWTKGFKS  
SGVEGRDVVALIRKAIQRRGDFDIDIVAVVNDTVGTMTCGYDDHNCEIGLIVGTGSNA  
CYMEEMRHIDMVEGDEGRMCINMEWGAFGDDGSLNDIRTEFDQEIDMGSLNPGKQLF  
EKMISGMYMGELVRLILVKMAKEELLFGGKLSPELLNTGRFETKDISDIEGEKDGIRKAR  
EVLMLRLGLDPTQEDCVATHRICQIVSTRSASLCAATLA AVLQRIKENKGEERLRSTIGVD  
GSVYKKHPHFAKRLHKTVRRLVPGCDVRFLRSEDGSGKGAAMVTAVAYRLADQHRAR  
QKTLEHLQLSHDQLLEV KRRMKVEMERGLSKETHASAPVKMLPTYVCATPDGTEKGDF  
LALDLGGTNFRVLLVRVRNGKWGGVEMHNKIYAIPQEV MHGTGDELFDHIVQCIADFLE  
YMG MKGVSLPLGFTFSFPCQQNSLDESILLKWT KGFKASGCEGEDVVTLLKEAIHRREE  
FDLDVVAVVNDTVGTMTCGFEDPHCEVGLIVGTGSNACYMEEMRNVELVEGEEGRM  
CVNMEWGAFGDNGCLDDFRTEFDVAVDELSL NPGKQRF EK MISGMYLGEIVRNILIDFT  
KRGLLFRGRISERLKTRGIFETKFLSQIESDCLALLQVRATLQHLGLESTCDDSIIVKEVCT  
VVARRAAQLCGAGMAAVVDRIENRGLDALKVTVGVDGTLYKLHPHFAKVMHETVKDL  
APKCDVSFLQSEDGSGKGAALITAVACRIREAGQR

SEQID No:237

CDGQPDCADGSDEWDCSYVLPRKVITA AAVIGSLVCGLLLVIALGCTCKLYAIRTQEYSIF  
APLSRMEAEIVQQQAPPSYGQLIAQGAIPPVEDFPTENPNDNSVLGNLRSLLQILRQDM  
TPGGGPGARRRQRGRLMRRLVHRLRRWGLLPRTNTPARASEARSQVTPSAAPLEALD  
GGTGPAREGGAVGGQDGEQAPPLPIKAPLPSASTSPAPTTVPEAPGPLPSLPLEPSLLS  
GVVQALRGRLLPSLGPPGPTRSPPGPHTAVLALEDEDDVLLVPLAEPGVWVAEAEDEP  
LLT

SEQID No:238

VTIAFLRLITTLVKGQLGSTQSQGLVPCVMFVLKEMLP SYHKWRYNSHGVREQIGCLILE  
LIHAILNLCHETDLHSSHTPSLQFLCICSLAYTEAGQTVINIMGIGVDTIDMVMAAQPRSD  
GAEGQGQGQLLIKTVKLAFSVTNNVIRLKPPSNVVSPLEQALSQHGAGHGNLI AVLAKYI  
YHKHDPALPRLAIQLLKRLATVAPMSVYACLGNDAAAIRDAFLTRLQSKIEDMRIKVMILE



FLTVAVETQPGLIELFLNLEVKDGSDGSKEFSLGMWSCLHAVLELIDSQQQDRYWCPPL  
 LHRAAIAFLHALWQDRRDSAMLVLRTKPKFWENLTSPLFGTLPSPSETSEPSILETCALI  
 MKIICLEIYYVVKGS LDQSLKDTLKKFSIEKR FAYWSGYVKSLAVHVAETEGSSCTSLEY  
 QMLVSAWRMLLIIATTHADIMHLTDSVVRRLFLDVLDGTKALLVPASVNCLRLGSMKC  
 TLLILLRQWKRELGSVDEILGPLTEILEGV LQADQQLMEKTKAKVFSAFITVLQMKEMKV  
 SDIPQYSQVLNV CETLQEEVIALFDQTRHSLALGSATEDKDSMETDDCSRSRHRDQR  
 DGVCVLGLHLAKELCEVDEDGDSWLQVTRRLPILPTLLTTLEVSLRMKQNLHFTEATLHL  
 LLTLARTQQGATAVAGAGITQSICLPLLSVYQLSTNGTAQTPSASRKSLDAPSWPGVYR  
 LSMSLMEQLLKTLYRNFLPEALDFVG VHQERTLQCLNAVRTVQSLACLEEADHTVGFIL  
 QLSNFMKEWHFHLPLQLMRDIQVGAQDGVLESGVMLGDREAVRSHWGTPSELQDVPE  
 RGLFPWGAQGLLSCAYSG

SEQID No:239

MWERLNCAAEDFYSRLLQKFNEEKKGIRKDPFLYEADVQVQLISKGQPNPLKNILNENDI  
 VFIVEKVPLEKEETSHIEELQSEETAISDFSTGENVGPLALPVGKARQLIGLYTMAHNPN  
 MTHLKINLPVTALPPLWVRCDSSDPEGTCWLGAELITTNNSITGIVLYVVSCKADKNYSV  
 NLENLKNLHKKRHHLSVTSTKGFAQYELFKSSALDDTITASQTALDISWSPVDEILQIP  
 PLSSTATLNKIVESGEPRGPLNHLYRELKFLVLADGLRTGVTEWLEPLEAKSAVELVQE  
 FLNDLNKLDGFGDSTKKDTEVETLKHDTAAVDRSVKRLFKVRSDLDFAEQLWCKMSSS  
 VISYQDLVKCFTLIIQSLQRGDIQPWLHSGSNSLLSKLIHQSYHGTMDTVSLSGTIPVQML  
 LEIGLDKLKKDYISFFIGQELASLNHLEYFIAPSVDIQEQVYRVQKLHHILEILVSCMPFIKS  
 QHELLFSLTQICIKYYKQNPLDEQHIFQLPVRPTAVKNLYQSEKPQKWRVEIYRGQKKIK  
 TVWQLSDSSPIDHLNFHKPDFSELTLNGSLEERIFFTNMVTCSQVHFK

SEQID No:240

MPGMVLFGRRWAIASDDLVPFGFFELVVRVLWWIGILTLYLMHRGKLD CAGGALLSSYL  
 IVLMILLAVVICTVSAIMCVSMRG TICNPGPRKSMSKLLYIRLALFFPEMVWASLGAAWVA  
 DGVQCDRTVVNGI IATVVVSWIIIAATVVSIIIVFDPLGGKMAPYSSAGPSHLD SHDSSQLL  
 NGLKTAATSVWETRIKLLCCCIGKDDHTRVAFSSSTAELFSTYFSDTDLVPSDIAAGLALLH  
 QQQDNIRNNQEPAQVVCHAPGSSQEADLDAELENCHHYMQFAAAAYGWPLYIYRNPL  
 TGLCRIGGDCCRSRTTDYDLVGGDQLNCHFGSILHTTGLQYRDFIHVSFHDKVYELPFL  
 VALDHRKESVVAVRGTM SLQDVLTDLSAESEVLDVECEVQDRLAHKGISQAARYVYQ  
 RLINDGILSQAFSIAPEYRLVIVGHSLGGGAAALLATMLRAAYPQVRCYAFSPPRGLWSK  
 ALQEYSQS FIVSLVLGKDVIPRLSVTNLEDLKRRILRVVAHCNKP KYKILLHGLWYELFGG

NPNNLPTELDGGDQEVLTQPLLGEQSLLTRWSPAYSFSSDSPLDSSPKYPPLYPPGRII  
HLQEEGASGRFGCCSAAHYSAKWSHEAEFSKILIGPKMLTDHMPDILMRALDSVVSDR  
AACVSCPAQGVSSVDVA

SEQID No:241

MSSKEVKTALKSARDAIRNKEYKEALKHCKTVLKQEKNNNYNWVFIGVAAAELEQPDQA  
QSAYKKAAELEPDQLLAWQGLANLYEKYNHINAKDDLPGVYQKLLDLYESVDKQKWCD  
VCKKLVDLYYQEKKHLEVARTWHKLIKTRREQGAENEELHQLWRKLTQFLAESTEDQN  
NETQQLLFTAFENALGLSDKIPSEDHQVLYRHFIQSLSKFPHESARLKKACEGMINIYPTV  
QYPLEVLCLEHIESGNLTDEGQQYCCRLVEMDSKSGPGLIGLGIKALQDKKYEDAVRNL  
TEGLKESPVCTSGWYHLAEAQVKMHRPKEAVLSCSQALKIVDNLGASGNSLYQRNLCL  
HLKAEALIKLSDYDSSEEAIRTLDDQISDADNIPGLLVLKSLAYRNKGSFDEAAKIMEDLLSS  
YPLAEVHALEALIHFTKKDYLQAEKCFQRALEKDTEVAEYHYQLGLTYWFMGEETRKD  
KTKALTHFLKAARLDTYMGKVFCYLGHYRDVVGDKNRARGCYRKAFELDDTDAESGA  
AAVDLSVELEDMEMALAILTTVTQKASAGTAKWAWLRRGLYYLKAGQHSQAVADLQAA  
LRADPKDFNCWESLGEAYLSRGGYTTALKSFTKASELNPESIYSVFKVAAIQQILGKYKE  
AVAQYQMIIKKKEDYVPALKGLGECHLMMAKAALVDYLDGKAVDYIEKALEYFTCALQH  
RADVSCLWKLAGDACTCLYAVAPSKVNVHVLGVLLGQKEGKQVLKKNELLHLGGRCY  
GRALKLMSTSNWCDLGINYYRQAQHLAETGSNMNDLKELLEKSLHCLKKAVRLDSNN  
HLYWNAALGVVACYSYGIGNYALAQHCIFIQSEQINAVAWTNLGVLYLTNENIEQAHEAF  
KMAQSLDPSYLMCWIGQALIAEAVGSYDTMDLFRHTTELNMHTEGALGYAYWVCTTLQ  
DKSNRETELYQYNILQMNAIPAAQVILNKYVERIQNYAPAFTMLGYLNEHLQLKKEAANA  
YQRAILLQTAEDQDTYNVAIRNYGRLLCSTGEYDKAIQAFKSTPLEVLEDIIGFALALFM  
KGLYKESSKAYERALSIVESEQDKAHILTALAITHEYKQGKTDVAKTLLFKCSILKEPTTESL  
QALCALGLAMQDATLSKAALNELLKHIKHKDSNYQRCLLTSIYALQGRSVAVQKQISKA  
VHSNPGDPALWSLLSRVVAQYAQRNAKGGVVAGNVAHILDSNHGKKALLYTAVNQLA  
MGSSSAEDEKNTALKTIQKAALLSPGDPAIWAGLMAACHADDKLALVNNTQPKRIDLYL  
ALLSAVSASIKDEKFFENYNQSLEKWSLSQAVTGLIDTGRISEAETLCTKNLKSNDPDQPA  
VILLRQVQCKPLLESQKPLPDAVLEELQKTVMSNSTSVPAWQWLAHVYQSQGMMRA  
AEMCYRKSLQLASQRGSWGKLSLLRLALLALKVCMANISNDHWPSLVQEATTEALK  
LCFCPLAVLLQALLQFKRKMGARETRRLLEVVYQPGYPKSIASARWYLLRHLYAKDD  
YELIDVLVNNNAKTHGDTRALELNQRLSSQ

SEQID No:242

MGAAAGRSPHLGPAPARRPQRSLLLLQLLLLVAAPGSTQAQAAPFPELCSYTWEAVDT  
KNNVLYKINICGSVDIVQCGPSSAVCMHDLKTRTYHSVGDSVLRSATRSLLFNTTVSC  
DQQGTNHRVQSSIAFLCGKTLGTPEFVTATECVHYFEWRTTAACKKDIFKANKEVPCYV  
FDEELRKHDLNPLIKLSGAYLVDDSDPDTSLFINVCRDIDTLRDPGSQLRACPPGTAACL  
VRGHQAFDVGQPRDGLKLVKDRLLVLSYVREEAGKLDFCDGHSPAVTITFVCPSERRE  
GTIPKLTAKSNCRYEIEWITEYACHRDYLESKTCSLSGEQQDVSIDLTPLAQSGGSSYIS  
DGKEYLFYLNVCGETEIQFCNKKQAAVCQVKKSDTSQVKAAGRYHNQTLRYSDGDLTLI  
YFGGDECSSGFQRMSVINFEKNKTAGNDGKGTPVFTGEVDCTYFFTWDTEYACVKEK  
EDLLCGATDGKKRYDLSALVRHAEPEQNWEAVDGSQTETEEKHFFINICHRVLQEGKA  
RGCPEDA AVCAVDKNGSKNLGKFISPMKEKGNIQLSYSDGDDCGHGKKIKTNITLVCK  
PGDLESAPVLRTSGEGGCFYEFEWRTAAACVLSKTEGENCTVFDSQAGFSFDLSPLTK  
KNGAYKVETKKYDFYINVCGPVSVSPCQPD SGACQVAKSDEKTWNLGLSNAKLSYYD  
GMIQLNYRGGTPYNNERHTPRATLITFLCDRDAGVGFPEYQEEDNSTYNFRWYTSYAC  
PEEPLC VVTDPSTLEQYDLSSLAKSEGGLGGN WYAMDNSGEHVTWRKYVINVC RPL  
NPVPGCNRYASACQMKEYEKDQGSFTEVVSISNLGMAKTGPVVEDSGSLLLEYVNGSA  
CTTSDGRQTTYTTRIHLVCSRGRNLN SHPIFSLNWE CVVSFLWNTEAACPIQTTTDTDQA  
CSIRDPN SGFVFNLNPLNSSQGYNVSGIGKIFMFNVCGTMPVCGTILGKPASGCEAETQ  
TEELKNWKPARPVGIEKSLQLSTEGFITLTYKGPLSAKGTADAFIVRFVCNDDVYSGPLK  
FLHQDIDSGQGIRNTYFEFETALACVPSPVDCQVTDLAGNEYDLTGLSTVRKPWTAVDT  
SVDGRKR TFYLSVCNPLPYIPGCQGS AVGSCLVSEGNSWNLG VVQMSPQAAANGSLSI  
MYVNGDKCGNQRFSTRITFECAQISGSPAFLQDGC EYVFIWRTVEACP VVRVEGDNC  
EVKDPRHGNLYDLKPLGLNDTIVSAGEYTY YFRVCGKLSSDVCPTSDKSKVVSSCQEK  
REPQGFHKVAGLLTQKLTYENGLLKMNFTGGDTCHKVYQRSTAIFYCDRGTQRPVFL  
KETSDCSYLF EWRTQYACPPFDLTECSFKDGAGNSFDLSSLSRYSDNWEAITGTGDPE  
HYLINVCKSLAPQAGTEPCPPEAAACLLGGSKPVNLGRVRDGPQWRDGIIVLKYVDGDL  
CPDGIRKKSTTIRFTCSSESQVNSRPMFISAVEDCEYTFAWPTATACPMKSNEHDDCQVT  
NPSTGHLFDLSSLSGRAGFTAAYSEKGLVYMSICGENENCPPGVGACFGQTRISVGKA  
NKRLRYVDQVLQLVYKDGSPCPSKSGLSYKSVISFVCRPEAGPTNRPMLISLDKQTCTL  
FFSWHTPLACEQATECSVRNGSSIVDLSPLIHRTGGYEAYDESEDDASDTNPDFYINIC  
QPLNPMH AVPCPAGAAVCKVPIDGPPIDIGRVAGPPILNPIANEIYLN FESSTPCLADKHF  
NYTSLIAFHCKRGVSMGTPKLLRTSECDFVFEWETPVVCPDEV RMDGCTLTDEQLLYS  
FNLSSLSTSTFKVTRDSRTYSVGVCTFAVGPEQGGCKDGGVCLLSGTKGASFGRLQS  
MKLDYRHQDEAVVLSYVNGDRCP PETDDGVPCVFPFIFNGKSYEECIIESRAKLWCSTT



ADYDRDHEWGFCRHSNSYRTSSIIFKCODEDEDIGRPQVFSEVRGCDVTFEWKTKVVCP  
 PKKLECKFVQKHKTYDLRLLSSLTGSWSLVHNGVSYIINLCQKIYKGPLGCSEASICR  
 RTTTGDVQVLGLVHTQKLGVIQDKVVVTYSKGYPCGGNKTASSVIELTCTKTVGRPAFK  
 RFDIDSCTYYFSWDSRAACAVKPQEVQMVNGTITNPINGKSFSLSGDIYFKLFRASGDMR  
 TNGDNYLYEIQQLSSITSSRNPACSGANICQVKPNDQHFSRKVGTSKTKYYLQDGDLDV  
 VFASSSKCGKDKTKSVSSTIFFHCDPLVEDGIPEFSHETADCQYLFSWYTSAVCPLGVG  
 FDSENPGDDGQMHKGLSERSQAVGAVLSLLLVALTCCLLALLYKKERRETVISKLTTT  
 CRRSSNVSYKYSKVNKEEETDENETEWLMEEIQLPPPRQGKEGQENGHITTKSVKALS  
 SLHGDDQDSEDEVLTIPVVKVHSGRGAGAESSHPVRNAQSNAQEREDDRVGLVRGE  
 KARKGKSSSAQQKTVSSTKLVSFHDDSDDLLHI

SEQID No:243

MSDKMSSFLHIGDICSLEYAEGSTNGFISTLGLVDDRCVVQPETGDLNNPPKKFRDCLFK  
 LCPMNRYSQKQFWKAAKPGANSTTDAVLLNKLHHAADLEKKQNETENRKLLGTVIQY  
 GNVIQLLHLKSNKYLTVNKRLPALLEKNAMRVTLDEAGNEGSWFYIQPFYKLRSIGDSVV  
 IGDKVVLNPNVAGQPLHASSHQLVDNPGCNEVNSVNCNTSWKIVLFMKWSDNKDDILK  
 GGDVVRLFHAEQEKFLTCDEHRKKQHVFRLRTTGRQSATSATSSKALWEVEVVQHDPC  
 RGGAGYWNSLFRFKHLATGHYLA AEVDPDFEEECLEFQPSVDPDQDASRSRLRNAQE  
 KMOVSLVSVPEGNDISSIFELDPTTLRGGDSLVRNSYVRLRHLCNTWVHSTNIPIDKE  
 EEKPVMLKIGTSPVKEDKEAFAIVPVSPA EVRDLDFANDASKVLGSIAGKLEKGTITQNE  
 RRSVTKLLEDLVYFVTGGTNSGQDVLEVVFSSKPNRERQKLMREQNILKQIFKLLQAPFT  
 DCGDGPMLRLEELGDQRHAPFRHICRLCYRVLRHSQQDYRKNQEYIAKQFGFMQKQI  
 GYDVLAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRKNREPRFLDYLSDL CVSMNKSIP  
 VTQELICKAVLNPTNADILIETKLVL SRFEFEGVSSTGENALEAGEDEEEVWLFWRDSNK  
 EIRSKSVRELAQDAKEGQKEDRDVLSYYRYQLNLFARMCLDRQYLAIN EISGQLDVDLIL  
 RCMSDENLPYDLRASFCRLMLMHVDRDPQE QVTPVKYARLWSEIPSEIAIDDYDSSG  
 ASKDEIKERFAQTMEFVEEYLRDVVCQRFPFSDKEKNKLTFEVVNLARNLIYFGFYNFS  
 DLLRLTKILLAILDCVHVTTIFPISKMAKGEENKGNNDVEKLKSSNVMRSIHGVGELMTQV  
 VLRGGGFLPMTPMAAAPEGNVKQAEPEKEDIMVMDTKLKIIELQFILNVRLDYRISCLLCI  
 FKREFDESNSQTSETSSGNSSQEGPSNVP GALDFEHIEEQAEGIFGGSEENTPLDLDD  
 HGGRTFLRVLLH LTMHDYPPLVSGALQLLFRHFSQRQEVLQAFKQVQLLVTSQDVDNY  
 KQIKQDL DQLRSIVEKSELWVYKGQGPDETMDGASGENEHKKTEEGNNKPQKHESTS  
 SYNVRVVKEILIRLSKLCVQESASVRKSRKQQQRLLRNMGAAHVLELLQIPYEKAEDTK  
 MQEIMRLAHEFLQNFCAGNQQNQALLHKHINLFLNPGILEAVTMQHIFMNNFQLCSEINE



RVVQHFVHCIETHGRNVQYIKFLQTIVKAEGKFIKKCQDMVMAELVNSGEDVLVIFYNDR  
 ASFQTLIQMMRSEDRMDENSPLMYHIHLVELLAVCTEGKNVYTEIKCNSLLPLDDIVRV  
 VTHEDCIPEVKIAYINFLNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNNTSDRK  
 HADSILEKYVTEIVMSIVTTFFSSPFSQSTTLQTRQPVFVQLLQGVFRVYHCNWLMP  
 QKASVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKSHSIVQKTAMNWRLSARNAARR  
 DSVLAASRDYRNIIERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELLFPENTDARRKC  
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 DSENSTEELEPSPPLRQLEDHKRGEALRQVLVNRYYGNNVRPSGRRESLTSFGNGPLSA  
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 ILLAIALLEGNTTIQHSFFCRLTEDKKSEKFFKVIFYDRMKVAQQEIKATVTVNTSDLGNK  
 KKDDEVDRDAPSRKKAKEPTTQITEEVRDQLLEASAATRKAFTTFRREADPDDHYQPG  
 EGTQATADKAKDDLEMSAVITIMQPILRFLQLLCENHNRDLQNFLRCQNNKTNYNLVCE  
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 DIITALILNDINPLGKKRMDLVLELKNNASKLLLAIMESRHDSENAERILYNMRPKELVEVI  
 KKAYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQLARHNKELQSMLKPGGQVDG  
 DEALEFYAKHTAQIEIVRLDRTMEQIVFPVPSICEFLTKE SKLRIYYTTERDEQGSKINDFF  
 LRSEDLFNEMNWQKKLRAQPVLYWCARNMSFWSSISFNLAVLMNLLVAFFYPFKGVR  
 GGTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALIASTILRLIFSVGLQPTLFLLGAFNVCN  
 KIIFLMSFVGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLFVHEFFYSLLLFDLVYREE  
 TLLNVIKSVTRNGRSIILTAVLALILVYLFSIVGYLFFKDDFILEVDRLPNETAVPETGESLA  
 SEFLFSDVCRVESGENCSPAPREELVPAEETE QDKEHTCETLLMCIVTVLSHGLRSGG  
 GVGDLVRKPSKEEPLFAARVIYDLLFFFMVIIIIVNLIFGVIIIDTFADLRSEKQKKEEILKTTC  
 FIGLERDKFDNKTVTFEHHIKEEHNMWHYLCFIVLVKVKDSTEYTGPE SYVAEMIKERN  
 LDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRK  
 QKQRIGLLGHPPHMNVNPQQPA

SEQID No:244

GGRQRCQRGRSCGAREEEVEPGTARPPPAASAMDASLEKIADPTLAEMGKNLKEAVK  
 MLEDSQRRTEEENGKKLISGDIPGPLQGSGQDMVSILQLVQNLMHGDEDEEPQSPRIQ  
 NIGEQQGHMALLGHSLGAYISTLDKEKLRKLTTRILSDTTLWLCRIFRYENGCA YFHEEER  
 EGLAKICRLAIHSRYEDFVVDGFNVLYNKKPVIYLSAAARPGLGQYLCNQLGLPFPCLCR  
 VPCNTVFGSQHQMDVAFLEKLIKDDIERGRLPLLLVANAGTAAVGHTDKIGRLKELCEQ  
 YGIWLHVEGVNLATLALGYVSSSVLAAAKCDSMTMTPGPWLGLPAVPAVTLYKHDDPA  
 LTLVAGLTSNKPTDKLRALPLWLSLQYLGLDGFVERIKHACQLSQRLQESLKKVNYIKILV

EDELSSPVVFRFFQELPGSDPVFKAVPVPNMTPSGVGRERHSCDALNRWLGEQLKQ  
 LVPASGLTVMDLEAEGTCLRFSPLMATAAVLGTRGEDVDQLVACIESKLPVLCCTLQLRE  
 EFKQEVEATAGLLYVDDPNWSGIGVVRYEHANDDKSSLKSDPEGENIHAGLLKKLNELE  
 SDLTFKIGPEYKSMKSCLYVGMA SDNVDAAELVETIAATAREIEENSRLLENMTEVVRKG  
 IQEAQVELQKASEERLLEEGVLRQIPVVGSVLWNWFSPVQALQKGRTFNLTAGSLESTEP  
 YVYKAQGAGVTLPPTPSGSRTKQRLPGQKPKFKRSLRGSDALSETSSVSHIEDLEKVERL  
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SEQID No:245

EPCALTPGPSHLALTFLPSKPGARPQPEGASWDAGPGGAPSAWADPGEGGPSPMLLP  
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 SQGDLSVPSPPPDPDSFFTPSTPTKTTYALLPACGPHGDARDSEAELRDELDDSPPAS  
 PSGSYITADGDSWASSPSCSLSLAPAEGLDFPSGWGLSPQGSMVDERELHPAGTPE  
 PPSSESSLADSSSSWGQEGHFFDLDFLANDPMIPAALLPFQGS LIFQVEAVEVTPLSP  
 EEEEEEA VADPD PGGDLAGEGEEDSTSASFLQSLSDLSITEGMDEAFAFRDDTSAASS  
 DSDSASYAEADDERLYSGEPHAQATLLQDSVQKTEEEESGGGAKGLQAQDGT VSWAVE  
 AAPQTS DRGAYLSQRQELISEVTEEGLALGQESTATVTPHTLQVAPGLQVEVATR VTPQ  
 AGEETDSTAGQESAAMAMPQPSQEGISEILGQESVTAEKLPTPQEETSLTLC PDSPQ  
 NLKEEGGLDLPSGRKPVAAATIVPRQAKEDLTLPQDSAMTPPLPLQD TD LSSAPKPVAA  
 ATIVSQQAE EGLTLPQDSVMTPPLPLQDTELSSAPKPVAAATLV SQQAE EGLTLPQDSA  
 MTPPLPLQD TD LSSAPKPVAAATLV SQQAE EGLTLPQDSAMTPPLPLQD TD LSSAPKPV  
 AAATLV SQQAE EGLTLPQDSAMTPPLPLQD TD LSSAPKPVAAATIVSQQAE EGLTLPQD  
 SAMTPPLPLQD TD LSSAPKPVAAATIVSQQAE EGLTLPQDSAMTPPLPLQD TD LSSAPK  
 PVAAATPV SQQAE EGLTLPQDSAMTPPLPLQD TD LSSAPKPVAAATPV SQQAE EGLTL  
 PQDSAMTAPLPLQDTGPTSGPEPLAVATPQTLQAEAGCAPGTEPVATMAQQEVGEAL  
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 LPEPASGAGEEIAEALS RPGREACLEARAHTGDGAKPDSPQKETLEVENQQEGGLKLLA  
 QEHGPRSALGGAREVPDAPPAACPEVSQARLLSPAREERGLSGKSTPEPTLPSAVATE  
 ASLDSCPESSVGAVSSLDRGCPDAPAPTSAPTSQQPEPVLGLGSVEQPHEVPSVLGTP  
 LLQPPENLAKGQPSTPVDRPLGPDPSAPGTLAGAALPPLEPPAPCLCQDPQEDSVEDE  
 EPPGSLGLPPPQAGVQPA AAAVSGTTQPLGTGPRVSLSPHSPLLSPKVASMDAKDLAL  
 QILPPCQVPPPSGPQSPAGPQGLSAPEQQEDED SLEEDSPRALGSGQHSDSHGESSA  
 ELDEQDILAPQTVQCPAQAPAGGSEETIAKAKQSRSEKKARKAMSKLGLRQIQGVTRITI  
 QKSKNILFVIAKPDVFKSPASDTYVVFGEAKIEDLSQQVHKAAA EKFKVPSEPSALVPES

APRPRVRLECKEEEEEEEEVDEAGLELRDIELVMAQANVSRAKAVRALRDNHSDIVNA  
IMELTM

SEQID No:246

MLTTLPFGSVSVESKMNNKAGSFFWNLRQFSTLVSTSRTMRLCCLGLCKPKIVHSNW  
NILNNFHNRMQSTDIIRYLFQDAFIFKSDVGFQTKGISTLTALRIERLLYAKRLFFDSKQSL  
VPVDKSDDDELKKVNLNHEVSNEDVLTKETKPNRISSRKLSEECNSLSDVLDAFSKAPTF  
PSSNYFTAMWTIAKRLSDDQKRFEKRLMF SHPAFNQLCEHMMREAKIMQYKYLLFSLH  
AIVKLGIPQNTILVQTLLRVTQERINECDEICLSVLSTVLEAMEPCKNVHVLRTGFRILVDQ  
QVWKIEDVFTLQVVMKCIGKDAPIALKRKLEMKALRELD RFSVLNSQHMFEVLAAMNHR  
SLILLDECSKVVDNIHGCPLRIMINILQSCKDLQYHNLDLFKGLADYVAATFDIWKFRKVL  
FILILFENLGFRPVGLMDLFMKRIVEDPESLNMKNILSILHTYSSLNHVYKCQNKEQFVEV  
MASALTGYLHTISSENLLDAVYSFCLMNYFPLAPFNQLLQKDIISELLTSDDMKNAYKLHT  
LDTCLKLDDTVYLRDIALSLPQLPRELPSSHTNAKVAEVLSSLLGGEGHFSKDVHLP HNY  
HIDFEIRMDTNRNQVLPLSDVDTTSATDIQRLLTYISFAGLSELKS

SEQID No:247

LQLSVKMSVLISQSVINYVEEENIPALKALLEKCKDVDERNECGQTPLMIAAEQGNLEIVK  
ELIKNGANCNLEDLDNWTALISASKEGHVHIVEELLKCGVNLEHRDMGGWTALMWACY  
KGRTDVVELLLSHGANPSVTGLYSVYPIIWAAGRGHADIVHLLLQNGAKVNCSDKYGTT  
PLVWAARKGHLECVKHLLAMGADV DQEGANSMTALIVAVKGGYTQSVKEILKRNPVN  
LTDKDGNTALMIASKEGHTEIVQDLLDAGTYVNIPDRSGDTV LIGAVRGGHVEIVRALLQ  
KYADIDIRGQDNKTALYWAVEKGNATMVRDILQCNP DTEICTKDGETPLIKATKMRNIEV  
VELLLDKGAKVSAVDKKGDTPLHIAIRGRSRKLAELL LRNP KDGRLLYRPNKAGETPYNI  
DCSHQKSILTQIFGARHLSPTETDGDMLGYDLYSSALADILSEPTMQPPICVGLYAQWG  
SGKSFLLKKLEDEMKT FAGQQIEPLFQFSWLIVFLTLLLCGGLGLLFAFTVHPNLGIAVSL  
SFLALLYIFFIVIYFGGRREGESWNWAWVLSTRLARHIGYLELLLKLMFVNPPELPEQTTK  
ALPVRFLFTDYNRLSSVGGETSLAEMIATLSDACEREFGLATRLFRVFKTEDTQGKKK  
WKKTCCLPSFVIFLFIIGCIISGITLLAIFRVD PKHLTVNAVLISIASVVGLAFVLNCRTWWQ  
VLDSLLNSQRKRLHNAASKLHKLKSEGFMKVLKCEVELMARMAKTIDSFTQNQTRLVVI  
DGLDACEQDKVLQMLD TVRVLFSKGPFIASFDPHIIKAINQNLNSVLRDSNINGHDYM  
RNIVHLPVFLNSRGLSNARKFLVTSATNGDVPCSDTTGIQEDADRRVSQNSLGEMTKLG  
SKTALNRRD TYRRRQMQR TITRQMSFDLTKLLVTE DWFS DISPQTMRRLLNIVSVTGRL  
LRANQISFNWDRLASWINLTEQWPYRTSWLILYLEETEGIPDQMTLKT IYERISKNIPTTK



DVEPLLEIDGDIRNFEVFLSSRTPVLVARDVKVFLPCTVNLDPKLREIIADVRAAREQISIG  
 GLAYPPLPLHEGPPRAPSGYSQPPSVCSSTSFNNGPFAGGVVSPQPHSSYYSGMTGPQ  
 HPFYNRPFAPYLYTPRYYPGGSQHLISRPSVKTS�PRDQNNGLEVIKEDAAEGLSSPT  
 DSSRGSGPAPGPVLLNSLNVDAVCEKQIEGLDQSMPLQYCTTIKKANINGRVLAQC  
 NIDELKKEMNMNFGDWHLFRSTVLEMRNAESHVVPEDPRFLSESSSGPAPHGEPARR  
 ASHNELPHTELSSQTPYTLNFSFEELNTLGLDEGAPRHSNLSWQSQTTRTPSLSSLNS  
 QDSSIEISKLTDKVQAEYRDAYREYIAQMSQLEGGPGSTTISGRSSPHSTYYMGQSSSG  
 GSIHSNLEQEKGDSEPKPDDGRKSFLMKRGDVIDYSSSGVSTNDASPLDPITEEDEKS  
 DQSGSKLLPGKKSSERSSLFQTDLKLKGSGLRYQKLPSEDEDESGTEESDNTPLLKDDK  
 DRKAEGKVERVPKSPEHSAEPIRTFIKAKEYLSDALLDKKDSSDSGVRSSSESSPNHSLH  
 NEVADDSQLEKANLIELEDDSHSGKRGIPHSLSGLQDPIIARMSICSEDKKSPSECSLIAS  
 SPEENWPACQKAYNLNRTPTSTVTLNNNSAPANRANQNFDMEGIRETSQVILRPSSSP  
 NPTTIQENENLKSMTHKRSQRSSYTRLKDPPELHAAASSESTGFGEERESIL

SEQID No:248

MEAAPPGPWPLLLLLLLLLLALCGCPAPAAASPLLLFANRRDVRLVDAGGVKLESTIVVS  
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 GKKLYWTDSETNRIEVANLNGTSRKVLFWQDLDQPRAIALDPAHGYMYWTDWGETPRI  
 ERAGMDGSTRKIIVDSDIYWPNGLTIDLEEQKLYWADAKLSFIHRANLDGSFRQKVVEG  
 SLTHPFALTLSGDTLYWTDWQTRSIIHACNKRTGGKRKEILSALYSPMDIQVLSQERQPF  
 FHTRCEEDNGGCSHLCLLSPSEPFYTCACPTGVQLQDNGRTCKAGAEVLLLARRTDL  
 RRISLDTPDFTDIVLQVDDIRHAIADYDPLEGYVYWTDDEVRAIRRAYLDGSGAQTLVNT  
 EINDPDGIAVDWVARNLWTDGTGTDRIEVTRLNGTSRKILVSEDLDEPRAIALHPVMGLM  
 YWTDWGENPKIECANLDGQERRVLVNASLGWPNGLALDLQEGKLYWGDAKTDKIEVIN  
 VDGTKRRTLLEDKLPHFIFGFTLLGDFIYWTDWQRRSIIERVHKVKASRDVIIDQLPDLML  
 KAVNVAKVVGTPNPCADRNGGCSHLCCFTPHATRCGCPIGLELLSDMKTCIVPEAFLVFT  
 SRAAIHRISLETNNNDVAIPLTGVKEASALDFDVSNNHIYWTDVSLKTISRFRMNGSSVE  
 HVVEFGLDYPEGMAVDWMGKNLYWADTGTNRIEVARLDGQFRQVLVWRDLNPRSL  
 ALDPTKGYIYWTEWGGKPRIVRAFMDGTNCMTLVDKVGRANDLTIDYADQRLYWTDLD  
 TNMIESSNMLGQERVVIADDLPHPFGLTQYSDYIYWTDWNLHSIERADKTSGRNRTLQ  
 GHLD FVMDILVFHSSRQDGLNDCMHNNNGQCGQLCLAIPGGHRCGCASHYTLPSSRN  
 CSPPTTFLLFSQKSAISRMIPDDQHSPDLILPLHGLRNVKAIDYDPLDKFIYWVDGRQNIK  
 RAKDDGTQPFVLTSLSQGQNPDRQPHDLSIDIYSRTLFWTCEATNTINVHRLSGEAMGV  
 VLRGDRDKPRAIVVNAERGYLYFTNMQDRAAKIERAALDGTEREVLFTTGLIRPVALVVD



NTLGKLFWVDADLKRIESCDLSGANRLTLEDANIVQPLGLTILGKHLWIDRQQQMIE  
 EKTGDKRTRIQRVAHLTGIIHAVEEVSLLEFSAHPCARDNGGCSHICIAKGDGTPRCS  
 CPVHLVLLQNLLTCGEPPTCSPDQFACATGEIDCIPGAWRCDGFPECDDQSDEEGCPV  
 CSAAQFPCARGQCVDLRLRCDGEADCQDRSDEVDCDAICLPNQFRCASGQCVLKQQ  
 CDSFPDCIDGSDELMCEITKPPSDDSPAHSAGPVGIIILSLFVMGGVYFVCQRVVCQR  
 YAGANGPFPHEYVSGTPHVPLNFIAPGGSQHGPFTGIACGKSMMSSVSLMGGRGGVP  
 LYDRNHVTGASSSSSSSTKATLYPPILNPPSPATDPSLYNMDMFYSSNIPATARPYP  
 YIRGMAPPPTPCSTDVCDSDYSASRWKASKYYLDLNSDSDPYPPPPTPHSQYLSAEDS  
 CPPSPATERSYFHLFPPPPSPCTDSS

SEQID No:249

MDMFPLTWVFLALYFSRHQVRGQPDPPCGGRLNSKDAYITSPGYPDYPSHQNCE  
 WIVYAPEPNQKIVLNFNPHFEIEKHDCKYDFIEIRDGDSEADLLGKHCGNIAPPTIISGS  
 MLYIKFTSDYARQGAGFSLRYEIFKTGSEDCSKNFTSPNGTIESPGFPEKYPHNLDCTFT  
 ILAKPKMEILQFLIFDLEHDPLQVGEGDCKYDWLDIWDGIPHVGPLIGKYCGTKTPSEL  
 SSTGILSLTFHTDMAVAKDGFSARYLVHQEPLNFQCNVPLGMESGRIANEQISASST  
 YSDGRWTPQQSRLHGDDNGWTPNLDSNKEYLQVDLRFLTMLTAIATQGAISRETQNG  
 YYVKSYSKLEVSTNGEDWMVYRHGKNHKVFQANNDATEVVLNKLHAPLLTRFVRIRPQT  
 WHSGIALRLELFGCRVTDAPCSNMLGMLSGLIADSQISASSTQEYLWSPSAARLVSSRS  
 GWFPRIQAQPGEEWLQVDLGTPKTVKGVIIQGARGGDSITAVEARAFVRKFKVSYSLN  
 GKDWEYIQDPRTQQPKLFEGNMHYDTPDIRRFDPIPAQYVRVYPERWSPAGIGMRLEV  
 LGCDWTDKPTVETLGPTVKSEETTPYPTTEEATECGENCSFEDDKDLQLPSGFNCN  
 FDFLEPCGWMYDHAKWLRTTWASSSSPNDRTFPDDRNLRLQSDSQREGQYARLIS  
 PPVHLPRSPVCMFQYQATGGRGVALQVVREASQESKLLWVIREDDQGGGEWKHGRIILP  
 SYDMEYQIVFEGVIGKGRSGEIAIDDIRISTDVPLENCMEPISAFAGENFKVDIPEIHEREG  
 YEDEIDDEYEVDWSNSSSATSGSGAPSTDKEKSWLYTLDPILITIAMSSLGVLLGATCA  
 GLLLYCTCSYSGLSSRSCTTLENYNFELYDGLKHKVKMNHQKCCSEA

SEQID No:250

MVSRCSCLGVCCLLLSLLLLAAWEVGSQGLHYSVYEEARHGTFVGRIAQDLGLELAELV  
 QRLFRVASKRHGDLLEVNLQNGILFVNSRIDREELCGRSVECSIHLEVIVDRPLQVFHVD  
 VEVKDINDNPPRFSVTEQKLSIPESRLLDSRFPLEGASDADVGENALLTYKLSPNEYFVL  
 DIINKKDKDKFPVLVLRKLLDREENPQLKLLLTATDGGKPEFTGSVSLILVLDANDNAPIF  
 DRPVYEVKMYENQVNQTLVIRLNASDSDEGINKEMMYSFSSLVPPTIRRKFWINERTGEI

KVND AIDFEDSNTYEIHVDVTDKGNPPMVGHCTVLVELLDENDNSPEVIVTSLSLPVKED  
 AQVGTVIALISVSDHDSGANGQVTC SLTPHVPFKLVSTYKNYYSLVLDSALDRERSAY  
 ELVVTARDGGSPPLWATASVSVEVADVNDNAPAF AQSEYTVFVKENNPPGCHIFTVSA  
 WDADAQENALVSYSLVERRLGERSLSSYVSVHAESGKVYALQPLDHEELELLQFQVSA  
 RDGGVPPLG SNLT LQVFVLDENDNAPALLASPAGSAGGAVSELVLR SVVAGHVVAKVR  
 AVDADSGYN AWLSYELQSAAVGARIPFRVGLYTGEISTTRALDETDSPRQRLLVLVKDH  
 GEPSLTATATVLVSLVEGSQAPKASSRASVGV APEVALVDVNVYLIIAICAVSSLLVLTLL  
 YTALRCSAAPT EGACGPVKPTLVCSSAVG SWSYSQQRRQRVC SGEGLPKADLMAFSP  
 SLPPCPMVDVDGEDQSIGGDHSRKPRQPNDWRY SASLRAGMHSSVHLEEAGILRAG  
 PGGPDQQWPTVSSATPEPEAGEVSP PVGAGVNSNSWTFKYGP GNP KQSGPGELPK  
 FIIPGSPAII SIRQEPTNSQIDKSDFITFGKKEETKKKKKKKKGNKTQEKKKEKGNSTTDNSD  
 Q

SEQID No:251

MENGGAGTLQIRQVLLFFVLLGMSQAGSETGNFLVMEELQSGSFVGNLAKTLGLEVSE  
 LSSRGARVVSNDNKECLQLDTNTGDLLLREMLDREELCGSNEPCVLYFQVLMKNPTQF  
 LQIELQVRDINDHSPVFLEKEMLLEIPENSPVGAVFLLES AKDL DVGINAVKSYTINPN SH  
 FHV KIRVNPDNRKYPELVLDKALDYEERPELSFILTALDGGSPPRSGTALVRVVVDIND  
 NSPEFEQAFYEVKILENSILGSLVVTVSAWDLD SGTNSELSYTFSHASEDIRKTFEINQKS  
 GDITLTAPLD FEAIESYSIIIQATDGGGLFGKSTVRIQVMDVNDNAPEITVSSITSPIENTP  
 ETVVMVFRI RDRD SGDNGKMVCSIPEDIPFVLKSSVNYYTLETERPLDRESRAEYNITI  
 TVTDLGTPRLKTEHNITVLVSDVNDNAPAFTQT SYALFVRENNSPALHIGSISATDRDSG  
 TNAQVNYSLLPSQDPHLPLASLV SINADNGHLFALRSLDYEALQGFQFRVGATDHGSPA  
 LSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPWAAEPGYLVTKVVAVDGD SGQ  
 NAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATA  
 TLHVLLVDGFSQPYLPLPEAAPAQQAQADSLTVYLVVALASVSSLFLFSVLLFVAVRLCRR  
 SRAAPVGRCSVPEGPFPGHLVDVSGTGTL SQSYHYEVCVTGGSR SNKFKFLKPIIPNFL  
 PQSTGSEVEENPPFQNNLGF

SEQID No:252

MEASGKLICRQRQVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQRE  
 FSRRGVRVVS RGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLR FQVLLES PF EFF  
 QAELQVIDINDHSPVFLDKQMLVKVSESSPPGTTFPLKNAEDLDVGQNNIENYIISPNSYF  
 RVLTRKRS DGRKYPELVLDKALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVLDVND

NAPEFEQPFYRVQISEDSPVGFLVVKVSATDVDVDTGVNGEISYSLFQASEEIGKTFKINPL  
 TGEIELKKQLDFEKLQSYEVNIEARDAGTFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPE  
 NAPETVVALFSVSDLDSENGKISCSIQEDLPFLLKSAENFYTLLTERPLDRESRAEYNIT  
 ITVTDLGTPMLITQLNMTVLIADVNDNAPAFTQTSYTLFVRENNSPALHIRSVSATDRDSG  
 TNAQVTYSLLPPQDPHLPLTSLVSINADNGHLFALRSLDYEALQGFQFRVGASDHGSPA  
 LSSEALVRVVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQ  
 NAWLSYQLLKATELGFLGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATA  
 TLHVLLVDGFSQPYPPLPEAAPTQAQADLLTVYLVVALASVSSLFLFSVLLFVAVRLCRR  
 SRAASVGRCLVPEGPLPGHLVDMSGTRTLSQSYQYEVCLAGGSGTNEFKFLKPIIPNFP  
 PQCPGKEIQGNSTFPNNFGFNIQ

SEQID No:253

MKKLGRIHPNRQVLAFILMVFLSQVRLEPIRYSVLEETESGSFVAHLAKDLGLGIGELASR  
 SARVLSDDDKQRLQLDRQTGDLLLREKLDREELCGPIEPCVLHFQVFLEMPVQFFQGEL  
 LIQDINDHSPIFPEREVLLKILENSQPGTLFPLLIAEDLDVGSNGLQKYTISPNSHFHILTRN  
 HSEGKKYPDLVQDKPLDREEQPEFSLTLVALDGGSPPRSGTVMVRILIMDINDNAPEFV  
 HTPYGVQVLENSPLDSPIVRVLARDIDAGNFGSVSYGLFQASDEIKQTFSINEVTGEILLK  
 KKLDFEKIKSYHVEIEATDGGGLSGKGTVVIEVVDVNDNPPELISSLTSSIPENAPETVVS  
 IFRIRDRDSGSENGKMICSIPDNLPFILKPTLKNFYTLVTERPLDRETSAEYNITIAVTDLGTP  
 RLKTQQNITVQVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDRDSGTNAQVTY  
 SLLPPQDPHLPLASLVNADNGHLFALRSLDYEALQAFEFVRVGASDRGSPALSSEALV  
 RVLVLDTNDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQNAWLSYQ  
 LLKATEPGLFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATATLHVLLVD  
 GFSQPYPPLPEAAPAQQAQADSLTVYLVVALASVSSLFLFSVLLFVAVRLCRRSRAASVG  
 RCSVPEGPFPGHLVDVSGTGTLTSQSYQYEVCLTGDSGTGEFKFLKPIFPNLLVQDTGR  
 EVKENPKFRNSLVFS

SEQID No:254

MQRAREAEMMKSQVLFPFLLSLFCGAISQQIRYTIPEELANGSRVGKLAIDLGLSVREL  
 PTRKLRVSAEDYFNVSLESGDLLVNGRIDREKICGRKLECALEFETVAENPMNVFHVVV  
 VIQDINDNAPRFVAKGIDLEICESALPGVKFSLDSAQDADVEGNSLKLYTINPNQYFSLST  
 KESPDGSKYPVLLLEKPLDREHQSSHRLILTAMDGGDPPLSGTTHIWIRVTDANDNAPV  
 FSQEVYRVSLQENVPWGTSVLRVMATDQDEGINAEITYAFLNSPISTSLFNLNPNTGDIT  
 TNGTLDFEETSRYVLSVEAKDGGVHTAHCNVQIEIVDENDNAPEVTFMSFSNQIPEDSD

LGTVIALIKVRDKDSGQNGMVTCTQEEVPFKLESTSKNYYKLVIAGALNREQTADYNVT  
 IIATDKGKPALSSRTSITLHISDINDNAPVFHQASYVVHVSENNPPGASIAQVSASDPDLG  
 PNGRVSYASILASDLEPRELLSYVSVSPQSGVVFAQRAFDHEQLRAFELTLQARDQGSPA  
 LSANVSLRVLVGDLNDNAPRVLYPALGPDGSAFFDMVPRAAEPGYLVTKVVAVDADSG  
 HNAWLSYHVLQASEPGLFSLGLRTGEVRTARALGDRDAARQRLLVAVRDGGQPPLSA  
 TATLHLIFADSLQEVLPLDLSRPEPSDPQTELQFYLVALALISVLFLAVILAIALLRLRRSS  
 SLDTEGCFQTGLCSKSGPGVPPNHSEGTLPYSYNLCIAASHSAKTEFNLSNLTPEMAPPQ  
 DLLCDDPSMVVCASNEDHKIAYDPSLSSHQAPPNTDWRFSQAQRPGTSGSQNGDDTG  
 TWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQFTLQHVPDYRQ  
 NVYIPGSNATLTNAAGKRDGKAPAGGNGNKKKSGKKEKK

SEQID No:255

MGGSCAQRRRAGPRQVLFPLLLPLFYPTLSEPIRYSIPEELAKGSVVGNLAKDLGLSVLD  
 VSARKLRVSAEKLHFSVDAESGDLLVKNRIDREQICKERRRCELQLEAVVENPLNIFHVI  
 VVIEDVNDHAPQFDKKEIHLEIFESASAGTRLSLDPATDPDININSIKDYKINSNPYFSLMV  
 RVNSDGGKYPELSLEKLLDREEQRSHSLILTALDGGDPPRSATAHIEISVKDTNDNPPVF  
 SRDEYRISLSENLP PGSPVLQVTATDQDEGVNAEINYYFRSTAQSTKHMFSLDEKTGMI  
 KNNQSFD FEDVERYTMEVEAKDGGGLSTQCKVIIIEILDENDNSPEIIITSLSDQILENSPP  
 GMVVALFKTRDLDFGGNGEVR CNIEDIPFKIYSSSNYYKLVT DGALDREQTPEYNVTI  
 VATDRGKPPLSSSR SITLYVADINDNAPVFDQTSYVVHVAENNNPPGASIAQVSASDPDL  
 GLNGHISYSIVASDLEPLAVSSYVSVSAQSGVVFAQRAFDHEQLRAFALTLQARDHGGSP  
 TLSANVSLRVLVGDRNDNAPRVLYPALGPDGSAFFDMVPRSAEPGYLVTKVVAVDADS  
 GHNAWLSYHVLQASEPGLFSLGLRTGEVRTARALGDRDAARQRLLVAVRDGGQPPLS  
 ATATLHLVFADNLQEILPLDSDRPVLSDPQAE LQFYLVALALISVLFLAVILAIALLRLRRS  
 LSPATWDCFHPGLCVKSGPVVPPNYSEGTLPYSYNLCIAHTGTKEFNFLKCSVPLHSNE  
 DMVCSVSPGALIPPHGGEDLTSHPETLTSQAPPNTDWRFSQAQRPGTSGSQNGDDTG  
 TWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQFTLQHVPDYRQ  
 NVYIPGSNATLTNAAGKRDGKAPAGGNGNKKKSGKKEKK

SEQID No:256

MAAAAARVVLSSAARGGLWGFSESLIRGAAGRS LYFGENRLRSTQAATQVVLNVPET  
 RVTCL ESGLRVASEDSGLSTCTVGLWIDAGSRYENEKNNGTAHFLEHMAFKGTKKRSQ  
 LDLELEIENMGAHLNAYTSREQTVYYAKAFSKDLPRAVEILADI IQNSTLGEAEIERERGV  
 LREMQUEVETNLQEVVFDYLHATAYQNTALGRTILGPTENIKSISRKDLVDYITTHYKGPRI



VLAAGGVSHDELLDLAKFHFGDSLCTHKGEIPALPPCKFTGSEIRVRDDKMPLAHLAIA  
 VEAVGWAHPDTICLMVANTLIGNWDRSFGGGMNLSSKLAQLTCHGNLCHSFQSFNTSY  
 TDTGLWGLYMCESSTVADMLHVQKEWMRLCTSVTESEVARARNLLKTNMLLQLDG  
 STPICEDIGRQMLCYNRRIPPELEARIDAVNAETIREVCTKYIYNRSPAIAAVGPIKQLPDF  
 KQIRSNMCWLRD

SEQID No:257

MGAYLSQPNTVKCSGDGVGAPRLPLPYGFSAMQGWRVSMEDAHNCIPELDSETAMFS  
 VYDGHGGEEVALYCAKYLPIIKDQKAYKEGKLQKALEDAFLAIDAKLTTEEVIKELAQIA  
 GRPTEDEDEKEKVADEDDVDNEEAALLHEEATMTIEELLTRYGQNCHKGPPHSKSGGG  
 TGEEPGSQGLNGEAGPEDSTRETPSQENGPTAKAYTGFSSNSERGTEAGQVGEPGIP  
 TGEAGPSCSSASDKLPRVAKSKFFEDSEDESDEAEEDSEECSEEDGYSSEEAEN  
 EDEDDTEEAEDDEEEEEEMMVPGMGKEEPGSDSGTTAVVALIRGKQLIVANAGDS  
 RCVVSEAGKALDMSYDHKPEDEVELARIKNAGGKVTMDGRVNGGLNLSRAIGDHFYKR  
 NKNLPPEEQMISALPDIKVLTLTDDHEFMVIACDGIWNVMSSQEVVDFIQSKISQRDENG  
 ELRLSSIVEELLQCLAPDTSGDGTGCDNMTCIICFKPRNTAELQPESGKRKLEEVLS  
 EGAEENGNSDKKKKAKRD

SEQID No:258

MMETPLPKAPEKRQVTAIIFLLLLWEAGSATIKYSVLEERDSGSFVANLAKDLGLGVGEL  
 AARGARILSKGNKQYLQLERKSGNLLLKEKLDREELCGDIDPCILHFQMLLKNPVQFIQG  
 ELQLQDVNDHAPEFLENEILLKISEGSHPGTSFPLKIAQDLVDGSNTVQNYSTNSYFHL  
 FTRNHSDGKKYPELVLDQALDREEQPQLRLTLTALDGGSPPTGTSGVLIVVDINDNVP  
 EFAQRRYEYVQVPENTPIGSLVITVSARDLDAGTHGELSYSFFQYSNQIIQAFEINSITGEIR  
 FKKALDFEEIQSYHMEVEASDGGGLSGKCTVAIEVMDINDNAPELTMSLLISDILENSPET  
 VVAVFGISDPDSGNNGKMMCSIQDHLPLKPTLENFYTLTTEGALDRESRAEYNITITVT  
 DLGTPRLKTEYNITLRVSDVNDNAPAFQTQSYTLFVRENNSPALHIGSVSATDRDSGTN  
 AQVTYSLLPPQNPHLPLASLVSINTDNGHLFALRSLDYEALQEFEFVRVGASDRGSPALS  
 SEALVRVLVCWTPPTTTRPSCCTRCRTAPRPAPSWCPGRPSRATW

SEQID No:259

MLRMRTAGWARGWCLGCCLLLPLSFSLAAAKQLLRYRLAEEGPADVRIGNVASDLGIV  
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 PSQSWVDLFEGQVIVLDINDNTPTFPSPVLTLTVEENRPVGTLYLLPTATDRDFGRNGIE

RYELLQEPGGGGSGGESRRAGAADSAPYPGGGGNGASGGGGSGGSKRRLDASEGGG  
 GTNPGGRSSVFELQVADTPDGEKQPQLIVKGALDREQRDSYELTLRVRDGGDPPRSS  
 QAILRVLITDVNDNSPRFEKSVYEADLAENSAPGTPILQLRAADLDVGVNGQIEYVFGAA  
 TESVRLLRLDETSGWLSVLHRIDREEVNQLRFTVMARDRGQPPKTDKATVVLNIKDEN  
 DNVPSIEIRKIGRIPLKDG VANVAEDVLVDTPIALVQVSDRDQGENGVVTCTVVGDVPFQ  
 LKPASDTEGDQNKKKYFLHTSTPLDYEATREFNVVIVAVDSGSPSLSSKNSLIVKVGDTN  
 DNPPMFGQSVVEVYFPENNIPGERVATVLATDADSGKNAEIAYS LDSSVMGIFAIDPDS  
 GDILVNTVLDREQTDREYEFKVNADKKGIPVLQGSTTVIVQVADKNDNDPKFMQDVFTFY  
 VKENLQPNSPVGMVTVM DADKGRNAEMSLYIEENNNIFSIENTGTIYSTMSFDREHQT  
 TYTFRVKAVDGGDPPRSATATVSLFVMDENDNAPT VTL PKNISY TLLPPSSNVRTVVAT  
 VLATDSDDGINADLNYSIVGGNPFLFEIDPTSGVVSLVGKLTQKH YGLHRLVVQVND S  
 GQPSQSTTTVVHV FVNESVSNATAIDSQIARSLHIPLTQDIAGDPSYEISKQRLSIVIGVVA  
 GIMTVILIILIVVMARYCRSKNKNGYEAGKKDHEDFFTPQQHDKSKKPKKDKKNKKSKQP  
 LYSSIVTVEASKPNGQRYDSVNEKLSDSPSMGRYRSVNGGPGSPDLARHYKSSSPLPT  
 VQLHPQSPTAGKKHQAVQDLPPANTFVGAGDNISIGSDHCSEYSCQTNNKYSKQMRLH  
 PYITVFG

SEQID No:260

MEIGWMHNRQRQVLVFFVLLSLSGAGAE LGSYSVVEETERGSFVANLGKDLGLGLTE  
 MSTRKARIISQGNKQHLQLKAQTGDLLINEKLDREELCGPTEPCILHFQVLMENPLEIFQ  
 AELRVIDINDHSPMFTEKEMILKIPENSPLGTEFPLNHALDLDVGSNNVQNYKISPSSHFR  
 VLIHEFRDGRKYPELVLDKELDREEEPQLRLTLTALDGGSPPRSGTAQVRIEVDINDNA  
 PEFEQPIYKVQIPENSPLGSLVATVSARDLDGGANGKISYTLFQPSEDISKTLEVNPMTG  
 EVRLRKQVDFEMVTSYEVRIKATDGGGLSGKCTLLLQVVDVNDNPPQVTMSALTSPIPE  
 NSPEIVVAVFSVSDPD SGNNGKTISSIQEDLPFLKPSVKNFYTLVTERALDREARAEYNI  
 TLTVTDMGTPRLKTEHNITVQISDVNDNAPTFTQT SYTLFVRENNSPALHIGSVSATDRD  
 SGTNAQVTYSLLPPQDPHLPLASLV SINADNGHLFALRSLDYEALQA FEFVRVGATDRGS  
 PALSREALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDS  
 GQNAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPRS  
 ATATLHVLLVDGFSQPFLPLPEAAPGQTQANSLTVYLVVALASVSSLFLFSVLLFVAVRL  
 CRRSRAASVGRCSMPEGPFPGRLVDVSGTGTLSQSYQYEVCLTGGSETSEFKFLKPIIP  
 NFSP

SEQID No:261

MDEDVLTTLKILIIGESGVGKSSLLLRFTDDTFDPELAATIGVDFKVKTISVDGNKAKLAIW  
DTAGQERFRTLTPSYRGAQGVILVYDVTRRDTFVKLDNWLNELETYCTRNDIVNMLVG  
NKIDKENREVDRNEGLKFARKHSMLFIEASAKTCDGVQCAFEELVEKIIQTPGLWESEN  
QNKGVKLSHREEGQGGGACGGYCSVL

SEQID No:262

MESRDHNNPQEGPTSSSGRRRAVEDNHLLIKAVQNEVDVLVQQQLLEGGANVNFQEEE  
GGWTPLHNAVQMSREDIVELLRRHGADPVLRRKNGATPFILAAIAGSVKLLKLFLSKGAD  
VNECDFYGFTAFMEAAYGKVKALKFLYKRGANVNLRRKTKEDQERLRKGGATALMDA  
AEKGHVEVLKILLDEMGADVNAACDNMGRNALIHALLSSDDSDVEAITHLLLDHGADVNV  
RGERGKTPLILAVEKKHLGLVQRLLEQEHIEINDTSDSGKTALLLAVELKLKKIAELLCKR  
GASTDCGDLVMTARRNYDHSVLKVLLSHGAKEDFHPPAEDWKPQSSHWGAALKDLHR  
IYRPMIGKLKFFIDEKYKIADTSEGGIYLGIFYEKQEVAVKTFCEGSPRAQREVSCLOSSR  
ENSHLVTFYGSSESHRGHLFVCVTLCEQTLEACLDVHRGEDVENEDEFARNVLSSIFKA  
VQELHLSCGYTHQDLQPQNILIDSKKAAHLADFDKSIKWAGDPQEVKRDLEDLGRVLVY  
VVKKGSISFEDLKAQSNEEVVQLSPDEETKDILHRLFHPGEHVRDCLSDLLGHPFFWTW  
ESRYRTLNRVGNESDIKTRKSESEILRLLQPGPSEHSKSFDKWTTKINECVMKKMNKFY  
EKRGNFYQNTVGDLLKFIRNLGEHIDEKHKMKMLKIGDPSLYFQKTFPDLVIYVYTKLQ  
NTEYRKHFQTHSPNKPQCDGAGGASGLASPGC

SEQID No:263

MACSIVQFCYFQDLQAARDFLPHLREEILSGALRRDPSKSTDWEDDGWGAWEEENEP  
QEPEEEGNTCKTQKTSWLQDCVLSLSPTNDLMVIAREQKAVFLVPKWKYSDKGKEEM  
QFAVGWWSGLNVEEGECVTSALCIPLASQKRSSTGRPDWTCIVVGFTSGYVRFYTENG  
VLLLAQLLNEDPVLQLKCRTYEIPRHPGVTEQNEELSILYPAAIVTIDGFSLFQSLRACRN  
QVAKAAASGNENIQPPPLAYKKWGLQDIDTIIDHASVGIMTLSPFDQMKTASNIGGFNAA  
IKNSPPAMSQYITVGSNPFTGFFYALEGSTQPLLSHVALAVASKLTSALFNAASGWLGW  
KSKHEEEAVQKQKPKVEPATPLAVRFGLPDSRRHGESICLSPCNTLAAVTDDFGRVILL  
DVARGIAIRMWKGYRDAQIGWIQTVEDLHERVPEKADFSPFGNSQGSPSRVAQFLVIYAP  
RRGILEVWSTQQGPRVGAFNVGKHCRLLYPGYKIMGLNNVTSQSWQPQTYQICLVDPV  
SGSVKTVNVPFHLALSDDKKSERAKDMHLVKKLAALLKTKSPNLDLVETEIKELILDIKYP  
TKKQALESILASERLPFSCLRNTQTLMDTLKSQELESVDEGLLQFCANKLKLQLYESVS  
QLNSLDFHLDTPFSDNDLALLRLDEKELLKLQALLEKYKQENTRTNVRFSDDKDGVLP

VKTFLEYEYEKDVNLNKKISEEEYVALGSFFFWKCLHGESSTEDMCHTLESAGLSPQLL  
 LSLLLSVWLSKEKDILDKPQSICCLHTMLSLLSKMKVAIDETWDSQSVSPWWQQMRTA  
 CIQSENNGAALLSAHVGHSAQAISNNMTEKKFSQTVLGADSEALTDSEALS LDTEY  
 WKLLLKQLEDCLILQTLLHSGKNTQTSKVSSLQAEPLPRLSVKKLLEGGKGGIADSVAK  
 WIFKQDFSPEVLKLANEERDAENPDEPKEGVNRSFLEVSEMEMDLGAIPDLLHLAYEQF  
 PCSLELDVLHAHCCWEYVVQWNKDPEEARFFVRSIEHLKQIFNAHVQNGIALMMWNTF  
 LVKRFSAAATYLMDKVGKSPKDRLCRRDVGMSDTAMTSFLGSCDLLQILMEADVSRDEI  
 QVPVLDTEDAWLSVEGPISIVELALEQKHIHYPLVEHHSILCSILYAVMRFSCLKTVKPLSLF  
 DSKGKNAFFKDLTSIQLLPSGEMDPNFISVRQQFLLKVVSAAVQAQHSATKVKDPTTEEA  
 TPTPFGKDQDWPALAVDLAHLQVSEDVRRHYVGELYNYGVDHLGEEAILQVHDKEV  
 LASQLLVLTGQRLAHALLHTQTKEGMELLARLPPTLCTWLKAMDPODLQNTVEVPIATTA  
 KLVNKVIELLPEKHGQYGLALHLIEAVEAISLPSL

SEQID No:264

MTVSGPGTPEPRPATPGASSVEQLRKEGNELFKCGDYGGALAAAYTQALGLDATPQDQ  
 AVLHRNRAACHLKLEDYDKAETEASKAIEKDGGDVKALYRRSQALEKLGRLDQAVLDLQ  
 RCVSLEPKNKVFQEALRNIGGGQIQEKVRYMSSTDAKVEQMFQILLDPEEKGTEKKQKAS  
 QNLVVLAREDAGAEKIFRSNGVQLLQRLLDMGETDLMLAALRTLVGICSEHQSRVATL  
 SILGTRRVVSILGVESQAVSLAACHLLQVMFDALKEGVKKGFRGKEGAIIVDPARELKVLI  
 SNLLDLLTEVGVSGQGRDNALTLLIKAVPRKSLKDPNNSLTWVIDQGLKKILEVGGSLQ  
 DPPGELAVTANSRMSASILLSKLFDDLKCDARENFHRLCENYIKSWFEGQGLAGKLRA  
 IQTVSCLLQGPCDAGNRALELSGVMESVIALCASEQEEEQLVAVEALIHAAGKAKRASFI  
 TANGVSLLKDLYKCSEKDSIRIRALVGLCKLGSAGGTDFSMKQFAEGSTLKLAKQCRKW  
 LCNDQIDAGTRRWAVEGLAYLTFDADVKEEFVEDAAALKALFQLSRLEERSVLF AVASA  
 LVNCTNSYDYEEPDPKMVELAKYAKQHVP EQHPKDKPSFVRARVKKLLAAGVVSAMVC  
 MVKTESPVLTS SCRELLSRVFLALVEEVEDRGTVVAQGGGGRALIPLALEGTDVGQTKAA  
 QALAKLTITSNPEMTFPGERIYEVVRPLVSLHLNCSGLQNFEALMALTNLAGISERLRQ  
 KILKEKAVPMIEGYMFEEHEMIRRAATECMCNLAMSKEVQDLFEAQGNDRLLKLLVLYSG  
 EDELLQRAAAGGLAMLTSMRPTLCSRIPQVTTHWLEILQALLSSNQELQHRGAVVVL  
 NMVEASREIASTLMESEMMEILSVLAKGDHSPVTRAAAACLDKAVEYGLIQPNQDGE

SEQID No:265

MRPEPGGCCCRRTVRANGCVANGEVRNGYVRSSAAAAAAAAAAGQIIHVTQNGGLYK  
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QDFENFYTRNLYMRIRDNWNRPICSVPGARVDIMERQSHDYNWSFKYTGNIIKGVINMG  
 SYNLYGFARNTGSCQEAAAKVLEEYAGVCSTRQEIGNLDKHEELEELVARFLGVEAA  
 MAYGMGFATNSMNIPALVGKGCLILSDELNHASLVLGARLSGATIRIFKHNNMQSLEKLL  
 KDAIVYGQPRTRRPWKKILILVEGIYSMEGSIVRLPEVIALKKKYKAYLYLDEAHSIGALGP  
 TGRGVVEYFGLDPEDVDVMMGTFTKSFGASGGYIGGKKELIDYLRTHSHSAVYATSLS  
 PPVVEQIITSMKCIMGQDGTSLGKECVQQLAENTRYFRRRLKEMGFIIYGNEDESPVVPL  
 MLYMPAKIGAFGREMLKRNIGVVVVVGFPATPIESRARFCLSAAHTKEILD TALKEIDEVG  
 DLLQLKYSRHRLVPLLD RPFDETTYEETED

SEQID No:266

MSGELPPNINIKEPRWDQSTFIGRANHFFTVTDPRNILLTNEQLESARKIVHDYRQGIVP  
 PGLTENELWRAKYIYDSAFHPDTGEKMILIGRMSAQVPMNMTITGCMMTFYRTTPAVLF  
 WQWINQSFNAVNYTNRSGDAPLTVNELGTAYVSATTGAVATALGLNALT KHV SPLIGR  
 FVPFAAVAAANCINIPLMRQRELKVGIPVTDENG NR LGESANA AKQAITQVVVSRILMAA  
 PGMAIPPFIMNTLEKKAFLKRFPWMSAPIQVGLVG FCLVFATPLCCALFPQKSSMSVTSL  
 EAELQAKIQESHPELRRVYFNKGL

SEQID No:267

MSQWYELQQLDSKFLEQVHQLYDDSFPM EIRQYLAQWLEKQDWEHAANDVSFATIRF  
 HDLLSQLDDQYSRFSLENNFLLQHNIRKSKRNLDNFQEDPIQMSMIIYSCLKEERKILE  
 NAQRFNQAQSGNIQSTVMLDKQKELDSKVRNVKDKVMCIEHEIKSLEDLQDEYDFKCK  
 TLQNREHETNGVAKSDQKQEQLLLKKMYLMLDNKRKEVVHKIIELLNVTELTQNALINDE  
 LVEWKRRRQQSACIGGPPNACLDQLQNWFTIVAESLQQVRQQLKKLEELEQKYTYEHDP  
 ITKNKQVLWDRTFSLFQQLIQSSFVVERQPCMPHTHPQRPLVLKTGVQFTVKLRLLVKLQ  
 ELNYNLKVKVLFDKDVNERNTVKGFRKFNILGTHTKVMNMEESTNGSLAAEFRHLQLKE  
 QKNAGTRTNEGPLIVTEELHSLSFETQLCQPGLVIDLETTSLPVVVISNVSQLPSGWASIL  
 WYNMLVAEPRNLSFFLT PPCARWAQLSEVLSWQFSSVTKRGLNVDQLNMLGEKLLGP  
 NASPDGLIPWTRFCKENINDKNFPFWLWIESILELIKHLPLWNDGCIMGFISKERERAL  
 LKDQQPGTFLLRFSSESSREGAITFTWVERSQNGGEPDFHAVEPYTKKELSAVTFPDIIR  
 NYKVMAAENIPENPLKYLYPNIDKDHAFGKYYSRPKEAPEPEMELDGP KGTGYIKTELISV  
 SEVHPSRLQTTDNLLPMSPEEFDEVSRIVGSVEFDSMMNTV

SEQID No:268

MEAVLNELVSVEDLLKFEKKFQSEKAAGSVSKSTQFEYAWCLVRTRYND DIRKGIVLLE

ELLPKGSKEEQRDYVFYLA VGN YRLKEYEKALKYVRG LLQTEPQNNQAKELERLIDKAM  
KKDGLVGMAIVGGMALGVAGLAGLIGLAVSKSKS

SEQID No:269

MGAVARAHGGLRVARARESVAGGRHRGAGRPGARAAGAAAGLVRAEAGGRRAGRG  
RRPGRGLPTGGGGGLAAA VGREVAQGLCDAIRLDGG LDLLRLLQAPELETRVQAARL  
LEQILVAENRDRVARIGLG VILNLAKEREPVELARSVAGILEHMFKHSEETCQRLVAAGG  
LDAVLYWCRRTPALLRHCALALGN CALHG GQAVQRRMVEKRAAEWLFPLAFSKEDE  
LLRLHACLAVAVLATNKEVEREVERSGTLALVEPLVASLDPGRFARCLVDASDTSQGRG  
PDDLQRLVPLLD SNRLEAQCIGAFYLCAEAAIKSLQGKTKVFSDIGAIQSLKRLVSYSTNG  
TKSALAKRALRLLGEEVPRPILPSVPSWKEAEVQTWLQQIGFSKYCESFREQQVDGDLL  
LRLTEEELQTD LGMKSGITRKRFFRELTELKTFANYSTCDRSNLADWLGS LDPRFRQYT  
YGLVSCGLDRSLLHRVSEQQLLED CGIHLGVHRARILTAAREMLHSPLPCTGGKPSGDT  
PDVFISYRRNSGSQLASLLKVHLQLHGFSVFIDVEKLEAGKFEDKLIQSVMGARNFVLVL  
SPGALDKCMQDHDCKDWVHKEIVTALSCGKNIVPIIDGFEWPEPQVLPEDMQAVLTFN  
GIKWSHEYQEATIEKIIRFLQGRSSRDSSAGSDTSLEGAAPMGPT

SEQID No:270

MVGEEKMSLRNRLSKSRENPEEDEDQRNPAKESLETPSNGRIDIKQLIAKKIKLTAEAE  
LKPFFMKEVGSHFDDFVTN LIEKSASLDNGGCALTTF SVLEGEKNNHRAKDLRAPPEQG  
KIFIARRSLLDELLEVDHIRT IYHMFIAL LILFILSTLVVDYIDEGRLVLEFSLLSYAFGKFPTV  
VWTWWIMFLSTFSVPYFLFQHWATGYSSSHPLIRSLFHGFLFMIFQIGVLGFGPTYVVL  
AYTLPPASRFIIIFEQIRFVMKAHSFVRENVPRVLNSAKEKSSTVPIPTVNQYLYFLFAPT  
YRDSYPRNPTVRWGYVAMKFAQVFGCFFYVYYIFERLCAPLFRNIKQEPFSARVLVLCV  
FNSILPGVLILFLTFFAFLHCWLN AFAEMLRFGDRMFYKDWWNSTSYSNYYRTWNVVV  
HDWLYYYAYKDFLWFFSKRFKSAAMLAVFAVSAVVHEYALAVCLSFFYPVLFVLFMFFG  
MAFNFIVNDSRKKPIWNVLMWTS LFLGNGVLLCFYSQEWYARRHCPLKNPTFLDYVRP  
RSWTCRYVF

SEQID No:271

MKAMDVLPILKEKVAYLSGGRDKRGGPILTFPARSNHDRIRQEDLRRLISYLACIPSEEV  
CKRGFTVIVDMRGSKWDSIKPLLKILQESFPCCIHVALIIPDNFWQKQRTNFGSSKFEF  
ETNMVSLEGLTKVVDPSQLTPEFDGCLEYNHEEWIEIRVAFEDYISNATHMLSRLEELQ  
DILAKKELPQDLEGARNMIEEHSQ LKKKVIKAPIEDLDLEGQKLLQRIQSSESFPKKNSGS

GNADLQNLLPKVSTMLDRLHSTRQHHLHQMWHVRKLLKLDQCFQLRLFEQDAEKMFDWI  
 THNKGLFLNSYTEIGTSHPHAMELQTQHNHFAMNCMVYVNINRIMSVANRLVESGHY  
 ASQQIRQIASQLEQEWKAFAAALDERSTLLDMSSIFHQKAEKYMSNVDSWCKACGEVD  
 LPSELQDLEDAIH HHQGIYEHITLAYSEVSQDGKSLDKLQRPLTPGSSDSL TASANYSK  
 AVHHVLDVIHEVLHHQRHVRTIWQHRKVRLHQRLQLCVFQQEVQQVLDWIENHGEAFL  
 SKHTGVGKSLHRARALQKRHEDFEEVAQNTYTNADKLEAAEQLAQTGECDPEEIYQA  
 AHQLEDRIQDFVRRVEQRKILLDMSVSFHTHV KELWTWLEELQKELLDDVYAESVEAVQ  
 DLIKRFQGGQQQTTLQVTNVVIKEGEDLIQQLRDSAISSNKTPHNSSINH IETVLQQLDEAQ  
 SQMEELFQERKIKLELFLHVRIFERDAIDIISDLESWNDELSQQMNDFDTEDLTIAEQRLQ  
 HHADKALTMNNLTDFVIHQGDLLQYVNEVQASGVELLCDRDVDMATRVQDLLEFLHE  
 KQQELDLAAEQHRKHLEQCVQLRHLQAEVKQVLGWIRNGESMLNAGLITASSLQEA EQ  
 LQREHEQFQHAIEKTHQSALQVQQKAEAMLQANHYDMDMIRDCAEKVASHWQQLMLK  
 MEDRLKLVNASVAFYKTSEQVCSVLESLEQEYKREEDWCGGADKLGPNS ETDHVTPMI  
 SKHLEQKEAFLKACTLARRNADVFLKYLHRNSVNMPGMVTHIKAPEQQVKNILNELFQR  
 ENRVLHYWTMRKRRLDQCQQYVVFERSAKQALEWIHDNGEFYLSHTSTGSSIQHTQ  
 ELLKEHEEFQITAKQTKERVKLLIQLADGFCEKGHAHAAEIKKCVTAVDKRYRDFSLRME  
 KYRTSLEKALGISSDSNKSSKSLQLDIIPASIPGSEVKLRDAAHELNEEK RKKSARRKEFIM  
 AELIQTEKAYVRDLRECMDTYLWEMTSGVEEI PPGIVNKELIIFGNMQEIYEFHNNIFLKE  
 LEKYEQLPEDVGHCFTWADKFQMYVTYCKNKP DSTQLILEHAGSYFDEIQQRHGLAN  
 SISSYLIKPVQRITKYQLLLKELLTCCEEGKGEIKDGLEVMLSVPK RANDAMHL SMLEGF  
 DENIESQGELILQESFQVWDPKTLIRKGRERHLFLFEMSLVFSKEVKDSSGRSKYLYKSK  
 LFTSELGVTEHVEGDPCKFALWVGRTPTSDNKIVLKASSIENKQDWIKHIREVIQERTIHL  
 KGALKEPIHIPKTAPATRQKGRRDGEDLDSQGDGSSQPD TISIASRTSQNTLDSDKLSG  
 GCELTVVIHDFTACNSNELTIRRGQTVEVLERPHDKPDWCLVRTTDRSPAAEGLVPCGS  
 LCIAHSRSSMEMEGIFNHKDSL SVSSNDASPPASVASLQPHMIGAQS SPGPKRPGNTL  
 RKWLTSPVRRLLSSGKADGHVKKLAHKHKKSREVRKSADAGS QKDSDDSAATPQDETV  
 EERGRNEGLSSGTL SKSSSSGMQSCGEEEGEEGADAVPLPPPMAIQQH SLLQPDSQD  
 DKASSRLLVRPTSSETPSAAELVSAIEELVKSKMALED RPSSLLVDQGDSSSPS FNPSD  
 NSLLSSSSPIDEMEERKSSSLKRRHYVLQELVETERDYVRDLGYVVEGYMALMKEDGV  
 PDDMKGKDKIVFGNIHQIYDWHRDFFLGELEKCLE DPEKLGSLFVKHERRLHMYIAYCQ  
 NKPKSEHIVSEYIDTFFEDLKQRLGHRQLTDL LIKPVQRIMKYQLLLKDFLKYSKKASLD  
 TSELERAVEVMCIVPRRCNDMMNVGRLQGFDGKIVAQ GKLLLQDTFLVTDQDAGLLPR  
 CRERRIFLFEQIVIFSEPLDKKKKGFSMPGFLFKNSIKVSCLCLEENVENDPCKFALT SRTG  
 DVVETFILHSSSPSVRQTWIHEINQILENQRNFLNALT SPIEYQRNHSGGGGGGGGGSGAA

AGVGAAAAAGPPVAAAATVAAPAAAAAAPPARAGAGPPGSPSLSDTTPPCWSPLQPRA  
 RQRQTRCQSESSSSSNISTMLVTHDYTAVKEDEINVYQGEVVQILASNQQNMFLVFRAA  
 TDQCPAAEGWIPGFVLGHTSAVIVENPDGTLKKSTSWHTALRLRKKSEKKDKDGKREG  
 KLENGYRKSREGLSNKVSVKLLNPNIYDVPPEFVIPLSEVTCETGETVVLRRCRVCGRP  
 KASITWKGPEHNTLNNDGHYSISYSDLGEATLKIVGVTTEDDGIYTCIAVNDMGSASSA  
 SLRVLGPGMDGIMVTWKDNFDSFYSEVAELGRGRFSVVKKCDQKGTKRAVATKFEVVK  
 KLMKRDQVTHELGILQSLQHPLLVLGLLDTFETPTSILVLEMADQGRLLDCVVRWGS  
 LT  
 EGKIRAHLEGEVLEAVRYLHNCRIAHLDLKPENILVDESLAKPTIKLADFGDAVQLNTTYI  
 HQLLGNPEFAAPEIILGNPVSLTSDTWSVGVLTIVLLSGVSPFLDDSVETCLNICRLDF  
 SFPDDYFKGVVSQKAKEFVCFLQEDPAKRPSAALALQEQWLQAGNGRSTGVLDTSRLT  
 SFIERRKHQNDVRPIRSIKNFLQSRLLPRV

SEQID No:272

MRKGLRATAARCGGLGYLLQMLVLPALALLSASGTGSAAQDDDDFFHELPETFPSDPP  
 EPLPHFLIEPEEAYIVKNKPNLYCKASPATQIYFKCNSEWVHQKDHIVDERVDETSGLIV  
 REVSIEISRQQVEELFGPEDYWCQCVAWSSAGTTKSRKAYVRIAYLRKTFEQEPLGKEV  
 SLEQEVLLQCRPPEGIPVAEVEWLKNEDIIDPVEDRNFYITIDHNLIQARLSDTANYTCV  
 AKNIVAKRKSTTATVIVYVNGGWSTWTEWSVCNSRCGRGYQKRTRTCTNPAPLNNGGA  
 FCEGQSVQKIACTTLCPPVDGRWTPWSKWSTCGTECTHWRRRECTAPAPKNGGKDCD  
 GLVLQSKNCTDGLCMQTAPDSDDVALYVGIVIAVIVCLAISVVVALFVYRKNHRDFESDII  
 DSSALNGGFQPVNIKAARQDLLAVPPDLTSAAAMYRGPVYALHDVSDKIPMTNSPILDP  
 LPNLKIKVYNTSGAVSPQDDLSEFTSKLSPQMTQSLENEALS LKNQSLARQTDPSCTA  
 FGSFNSLGGHLIVPNSGVSLIPAGAIQQGRVYEMYVTVHRKETMRPPMDDSQTLLTPV  
 VSCGPPGALLTRPVVLTMHHCADPNTEDWKILLKNQAAQGWEDVVVVGEENFTTPC  
 YIKLDAEACHILTENLSTYALVGHSTTKAAAKRLKLAIFGPLCCSSLEYSIRVYCLDDTQD  
 ALKEILHLERQTGGQLLEPKALHFKGSTHNLRLSIHDIAHSLWKSLLAKYQEIPFYHV  
 WSGSQRNLHCTFTLERFSLNTVELVCKLCVRQVEGEGQIFQLNCTVSEEPTGIDLPLLD  
 PANTITVTGPSAFSIPPIRQKLCSSLDAPQTRGHDWRMLAHKLNLDRYLNYFATKSSP  
 TGVILDLWEAQNFDPGNLSMLAAVLEEMGRHETVVSLAAEGQY

SEQID No:273

MAVFVLLALVAGVLGNEFSILKSPGSVVFRNGNWPPIGERIPDVAALSMGFSVKEDLS  
 WPGLA VGNLFHRPRATVMVMVKG VNK LALPPGSVISYPLENAVPFSLDSVANSIHSLS  
 FS  
 EETPVVLQLAPSEERVYMGKANSVFEDLSVTLRQLRNRLFQENSVLSSLPLNSLSRNN



EVDLLFLSELQVLHDISSLLSRHKHLAKDHSPDLYSLELAGLDEIGKRYGEDSEQFRDAS  
 KILVDALQKFADDMYSLYGGNAVVELVTVKSFDTSLIRKTRTILEAKRAKNPASPYNLAY  
 KYNFEYSVVFNMVLWIMIALALAVIITSYNIWNMDPGYDSIIYRMTNQKIRMD

SEQID No:274

MTFYLFGIRSFPKLWKSPYLGLGPGHSYVSLFLADRCGIRNQQRLFSLKTMS PQNTKAT  
 NLIAKARYLRKDEGSNKQVYSVPHFFLAGAAKERSQMNSQTEDHALAPVRNTIQLPTQP  
 LNSEEWDKLKEDLKENTGKTSFESWIISQMAGCHSSIDVAKSLLAWVAAKNNGIVSYDL  
 LVKYLYLCVFHMQTSEVIDVFEIMKARYKTLEPRGYSLLIRGLIHSDRWREALLLLEDIKK  
 VITPSKKNYNDCIQGALLHQDVNTAWNLYQELLGHDIVPMLET LKAFFDFGKDIKDDNYS  
 NKLLDILSYLRNNQLYPGESFAHSIKTWFE SGGCSCGKTIESIQLSPEEYECLKGKIMR  
 DVIDGGDQYRKTTTPQELKRFENFIKSRPPFDVIDGLNVAKMFPKVR ESQLLLNVVSQ L  
 AKRNLRLLLVLGRKHMLRRSSQWSRDEMEEVQKQASCFFADDISEDDPFLLYATLHSGN  
 HCRFITRDLMRD HKACLPDAKTQRLFFKWQQGHQLAIVNRFP GSKLTFQRILSYDTVVQ  
 TTGDSWHIPYDEDLVERCSCEVPTKWLC LHQKT

SEQID No:275

MALALAALAAVEPACGSRYQQ LQNEEESGEPEQAAGDAPPPYSSISAESAAYFDYKDE  
 SGFPKPPSYNVATTLP SYDEAERTKAEATIPLVPGRDEDFVGRDDFDDADQLRIGNDGI  
 FMLTFFMAFLFNWIGFFLSFCLTTSAAGRYGAISGFGLSLIKWILIVRFSTYFPGYFDGQY  
 WLWWWVFLVLGFLFLRGFINYAKVRKMPETFSNLPRTRVLFY

SEQID No:276

MDPECAQLLPALCAVLVDPGQP VADDTCLEKLLDWFKTVTEGESSVLLQEHPCLVELL  
 SHVLKVQDLSSGVLSFSLRLAGTFAAQENCFQYLQQGELLPG LFGEPGPLGRATWAVP  
 TVRSGWIQGLRSLAQHPSALRFLADHGAVDTIFSLQGDSSLFVASAASQLLVHVLALSM  
 RGGAEGQPCLPGGDWPACAQKIMDHVEESLCSAATPKVTQALNVLT TTTFGRCQSPWT  
 EALWVRLSPRVACLLERDPIPAAHSFVDLLLCVARSPVFSSSDGSLWETVARALSCLGP  
 THMGPLALGILKLEHCPQALRTQAFQVLLQPLACVLKATVQAPGPPGLLDGTADDATTV  
 DTLLASKSSCAGLLCRTLAHLEELQPLPQRPSWPQASLLGATVTVLRLCDGSAAPASS  
 VGGHLCGTLAGCVRVQRAALDFLGTL SGGTG PQELVTQALAVLLECLESPGSSPTVLK  
 KAFQATLRWLLSSPKTPGCSDLGPLIPQFLRELFPVLQKRLCHPCWEVRDSALEFLTQL  
 SRHWGGQADFRCALLASEVPQLALQLLQDPESYVRASAVTAMGQLSSQGLHAPTSPE  
 HAEARQSLFLELLHILSV DSEGFP RRAVMQVFTEWLRDGHADAAQDTEQFVATVLQAA

SRDLWEVRAQGLELALVFLGQTLGPPRTHCPYAVALPEVAPAQPLTEALRALCHVGL  
FDFAFCALFDCDRPVAQKSCDLLFLRDKIASYSSLREARGSPNTASAEATLPRWRAGE  
QAQPPGDQEPEAVLAMLRSLDLEGLRSTLAESSDHVEKSPQSLLQDMLATGGFLQGDE  
ADCY

SEQID No:277

MVNYAWAGRSQRKLWWRSVAVLTCKSVVRPGYRGGLQARRSTLLKTCARARATAPG  
AMKMVAPWTRFYNSCCLCCHVRTGTILLGVWYLIINAVVLLILLSALADPDQYNFSSE  
LGGDFEFMDDANMCIAIAISLLMILICAMATYGAYKQRAAWIIPFFCYQIFDFALNMLVAIT  
VLIYPNSIQEYIRQLPPNFPYRDDVMSVNPTCLVLIILLFISIILTFKGYLISCVWNCYRYING  
RNSSDVLVYVTSNDTTVLLPPYDDATVNGAAKEPPPPYVSA

SEQID No:278

MNIFDRKINFDALLKFSHITPSTQQHLKKVYASFALCMFVAAAGAYVHMTTHFIQAGLLS  
ALGSLILMIWLMATPHSHETEQRGLLAGFAFLTGVGLGPALEFCIAVNPSILPTAFMGT  
AMIFTCFTLSALYARRRSYLFLGGILMSALSLLLLSSLGNVFFGSIWLFQANLYVGLVVMC  
GFVLFDTQLIEKAEHGDQDYIWHCIDLFLDFITVFRKLMMILAMNEKDKKKEKK

SEQID No:279

MASILDEYENSLSRSAVLQPGCPSVGIPHSGYVNAQLEKEVPIFTKQRIDFTPSEIRITSLV  
VSSNQLCMSLGKDTLLRIDLGKANEPNHVELGRKDDAKVHKMFLDHTGSHLLIALSSTE  
VLYVNRNGQKVRPLARWKQQLVESVGWNKALGTESSTGPILVGTAQGHIFEAEELSASE  
GGLFGPAPDLYFRPLYVLNEEGGPAPVCSLEAERGPDGRSFVIATTRQRLFQFIGRAAE  
GAEAQGFSGLFAAYTDHPPPFREFPSNLGYSELAFYTPKLRSAPRAFAWMMGDGVLY  
GALDCGRPDSLLSEERVWEYPEGVGPGASPPLAIVLTQFHFLLLLADRVEAVCTLTGQV  
VLRDHFLEKFGPLKHMVKDSSTGQLWAYTERAVFRYHVQREARDVWRTYLDMNRFDL  
AKEYCRERPDCLDTVLAREADFCFRQRRYLESARCYALTQSYFEEIALKFLEARQEEAL  
AEFLQRKLASLKPAERTQATLLTTWLTELYLSRLGALQGDPEALTLYREVRNLTQFHPLP  
LAPLLSLSFPTHVLFTSREREREHLSSVCSLCGLWNPSSSLSEEAFSSSCL

SEQID No:280

MTSATSPIILKWDPKSLEIRTLTVERLLEPLVTQVTTLVNTSNKGPSGKKKGRSKKAHVL  
AASVEQATQNFLEKGEQIAKESQDLKEELVAAVEDVRKQGETMRIASSEFADDPCSSVK  
RGTMVRAARALLSAVTRLLILADMADVMRLLSHLKIVEEAEAVKNATNEQDLANRFKEF

GKKMVKLNYVAARRQQELKDPHCRDEMAAARGALKKNATMLY TASQAFLRHPDVAAT  
 RANRDYVFKQVQEAIAGISNAAQATSPTDEAKGHTGIGELAAALNEFDNKIILDPMTFSE  
 ARFRPSLEERLESIISGAALMADSSCTRDDRRERIVAECNAVRQALQDLLSEYMNNTGR  
 KEKGDPLNIAIDKMTKKTRDLRRQLRKAVMDHISDSFLETNVPLLVLIEAAKSGNEKEVK  
 EYAQVFREHANKLVEVANLACISISNNEEGVKLVRMAATQIDSLCPQVINAALTLAARPQS  
 KVAQDNMDVFKDQWEKQVRVLTEAVDDITSVDDFLSVSENHILEDVNKCVIALQEGDVD  
 TLDRTAGAIRGRAARVIHIINAEMENYEAGVYTEKVL EATKLLSETVMPRFAEQVEVAIEA  
 LSANVPQPFEENE FIDASRLVYDGVRDIRKAVLMIRTPEELEDSDFEQEDYDVRRGTS  
 VQTEDDQLIAGQSARAIMAQLPQEEKAKIAEQVEIFHQEKSKLDAEVAKWDDSGNDIIVL  
 AKQMCMIMMEMTDFTRGKGPLKNTSDVINAACKIAEAGSRMDKLARAVADQCPDSACK  
 QDLLAYLQRIALYCHQLNICKSVKAEVQNLGGELIVSGTGVQSTFTTFYEVD CDVIDGGR  
 ASQLSTHLPTCAEGAPIGSGSSDSSMLDSATSLIQA AKNLMNAVVLTVKASYVASTKYQ  
 KVYGTA AVNSPVVSWKMKAPEKKPLVKREKPEEFQTRVRRGSQKKHISPVQALSEFKA  
 MDSF

SEQID No:281

MSGDSERAVAPGVVPAPCASKVELRLSCRHLLDRDPLTKSDPSVLLQQAQGQWLQV  
 DRTEVVKSSLHPVFSKVFTVDYYFEGVQKLRFEVYDTHGPSGLTCQDDDFLGGMECTL  
 GQIVAQKKMTRPLLLRFGRNAGKSTITVIAEDISGNNGYVELSFQARKLDDKDLFSKSDP  
 FLELYRVNDDGSEQLVYRTEVVKNNLNPVWEPFKVSLNSLCSCEETRPLKCLVWDYDS  
 RGKHDFIGDFTTTFAEMQKAFEEEEQQAQWDCVNAKYKQKKRNYKN SGVVILADLKLHR  
 VHSFLDYIMGGCQIHCTVAIDFTASNGDPRNSCSLHHINPYQPNEYLRALVAVGEVCQD  
 YDSDKRFSALGFGARIPPKYEVSHDFAINFPEDDECEGIQGVVEAYQNCLPKVQLYGP  
 TNVAPIISKVARMAAAEESTGEASQYYILLITDGVVTDMSDTREAI VRASHLPMSVIIVGV  
 GNADFTDMQILDGDDGVLRSPRGEPALRDIVQFVPFRELKNASPAALAKCVLAEV PKQV  
 VEYYSHKELPPRSLGAQTGEAAASSAP

SEQID No:282

MAAQCVTKVALNVSCANLLDKDIGSKSDPLCVLFLNTSGQQWYEVERTERIKNCLNPQF  
 SKTFIIDYYFEVVQKLKFGVYDIDNKTIELSDDDFLGECECTLGQIVSSKKLTRPLVMKTG  
 RPAGKGSITISAEI KDNRVVLFEMEARKLDNKNDLFGKSDPYLEFHKQTS DGNWLMVHR  
 TEVVKNNLNPVWRPFKISLNSLCYGDMDKTIKVECYDYDNDGSHDLIGTFQTTMTKLKE  
 ASRSSPVEFECINEKKRQKKKSYKNSGVISVKQCEITVECTFLDYIMGGCQLNFTVG VDF  
 TGSNGDPRSPDSLHYISPNGVNEYLTALWSVGLVIQDYDADKMFP AFGFGAQIPPQWQ

VSHEFPMNPNPSNPYCNGIQGIVEAYRSCLPQIKLYGPTNFSPIINHVARFAAAATQQQT  
 ASQYFVLLIITDGVITDLDETRQAIVNASRLPMSIIIVGVGGADFSAMEFLDGDGGSLRSPL  
 GEVAIRDIVQFVPFRQFQNAPEALAQCVLAEIPQQVVG YFNTYKLLPPKNPATKQQKQ

SEQID No:283

MAVSASPVISATSSGAGVPGGLFRAEPLYSTPREPPRLTPNMINSFVVNNHSNSAGGG  
 GRGNTNTNECRMVDMHGMKVASFLMDGQELICLPQVFDLFLKHLVGGLHTVYTKLKRL  
 DISPVVCTVEQVRILRGLGAIQPGVNRCKLITRKDFETLFTDCTNARRKRQMTRKQAVN  
 SSRPGRPPKRS LGVLQENARLLTHAVPGLLSPGLITPTGITAAAMAEAMKLQKMKLMAM  
 NTLQGNGSQNGTESEPDDLNSNTGGSESSWDKDKMQSPFAAPGPQHGHIAHAALAGQ  
 PGIGGAPTLNPLQQNHLLTNRLDLPFMMMPHPLLPSLPPASVAMAMNQMNHNTIAN  
 MAAAAQIHSPLSRAGTSVIKERIPESPSPAPSLEENHRPGSQTSSHTSSSVSSSPSQMD  
 HHLERMEEVPVQIPIMKSPLDKIQLTPGQALPAGFP GPFFIFADSLSSVETLLTNIQGLLKV  
 ALDNARIQEKQIQQEKELRLELYREREIRENLERQLAVELQSRTTMQKRLKKEKKT KRK  
 LQEALFESKRREQVEQALKQATTSDSGLRMLKDTGIPDIEIENNGTPHDSAAMQGGNY  
 YCLEMAQQLYSA

SEQID No:284

MDDSEVESTASILASVKEQEAQFEKLTRALEEERRHVSAQLERVRVSPQDANPLMANG  
 TLTRRHQNGRFVGDADLERQKFSDLKLNGPQDHSLLYSTIPRMQEPGQIVETYTEED  
 PEGAMSVVSVETSDDGTTRRTETTVKKVVKT VTTTRTVQPVAMGPDGLPVDASSVSNNY  
 IQTLGRDFRKNNGNGGPGPYVGQAGTATLPRNFHYPPDGYSRHYEDGYPGGSDNYGSL  
 SRVTRIEERYRPSMEGYRAPSRQDVYGPQPQVRVGGSSVDLHRFHPEPYGLEDDQRS  
 MGYDDL DYGMMSDYGTARRTGTPSDPRRRLRSYEDMIGEEVPSDQYYWAPLAQHER  
 GSLASLDSL RKGGPPPPNWRQPELPEVIAMLGFR LDAVKSNAAYLQHLCYRNDKVKT  
 DVRKLKGIPVLVGLLDHPKKEVHLGACGALKNISFGRDQDNKIAIKNCDGVPALVRLLRK  
 ARDMDLTEVITGTLWNLSSHDSIKMEIVDHALHALTDEVIIPHSGWEREPNEDCKPRHIE  
 WESVLTNTAGCLRVSSERSEARRKLRECDGLVDALIFIVQAEIGQKDSDSLKLVENCVC  
 LLRNLSYQVHREIPQAERYQEAAPNVANNTGPHAASCFGAKKGKGKKPIEDPANDTVD  
 FPKRTSPARGYELLFQPEVVRIYISLLKESKTPAILEASAGAIQNLCAGRWTYGRYIRSAL  
 RQEKALSAIADLLTNEHERVVKAASGALRNLA VDARNKELIGKHAIPNLVKNLPGGQQN  
 SSWNFSEDTVISILNTINEVIAENLEAAKKLRETQGIEKLV LINKSGNRSEKEVRAAALVLQ  
 TIWGYKELRKPLEKEGWKKSD FQVNLNNASRSQSSHSYDDSTLPLIDRNQKSDNNYST



PNERGDHNRTLDRSGDLGDMEPLKGTTPLMQDEGQESLEEELDVLVLDDEGGQVSYP  
SMQKI

SEQID No:285

MACPALGLEALQPLQPEPPPEPAFSEAQKWIEQVTGRSFGDKDFRTGLENGILLCELLN  
AIKPGLVKKINRLPTPIAGLDNIILFLRGCKELGLKESQLFDPSDLQDTSNRVTVKSLDYSR  
KLKNVLVTIYWLKGKAANSCTSYSGTTNLKEFEGLLAQMRKDTDDIESPKRSIRD SGYID  
CWDSERSDSLSPPRHGRDDSFDSLDSFGSRSRQTPSPDVVLRGSSDGRGSDSESDLP  
HRKLPDVKKDDMSARRTSHGEPKSAVPFNQYLPNKSNTAYVPAPLRKKKAEREEYR  
KSWSTATSPLGGERPFRYGPRTPVSDDAESTSMFDMRCEEEAAVQPHSRARQEQLQL  
INNQLREEDDKWQDDLARWKSRRRSVSQDLIKKEEERKKMEKLLAGEDGTSEERRKSIK  
TYREIVQEKERRERELHEAYKNARSQEEAEGILQQYIERFTISEAVLERLEMPKILERSHS  
TEPNLSSFLNDPNPMKYLRQQSLPPP KFTATVETTIARASVLDTSMSAGSGSPSKTVTP  
KAVPMLTPKPYSQPKNSQDVLKTFKVDGKVS VNGETVHREEEKERECPTVAPAHSLTK  
SQMFEGVARVHGSPLELKQDNGSIEINIKKPNSVPQELAAATTEKTEPNSQEDKNDGGKS  
RKGNIELASSE PQHFTTTVTRCSPTVAFVEFPSSPQLKNDVSEEKDQKKPENEMSGKV  
ELVLSQKVVKPKSPEPEATLTFFFLDKMPEANQLHLPNLNSQVDSPSSEKSPVMTPFKF  
WAWDPEEERRRRQEKWQQEQERLLQERYQKEQDKLKEEWEKAQKEVEEEEERRYYEE  
ERKIIEDTVVPFTVSSSSADQLSTSSSMTEGSGTMNKIDLGNCQDEKQDRRWKKSFGG  
DDSDLLLKTRES DRLEEKGSLTEGALAHSGNPVSKGVHEDHQLDTEAGAPHCGTNPQL  
AQDPSQNNQTSNPTHSSSE DVKPKTLPLDKSINHQIESPSERRRKKSPREHFQAGPFSPC  
SPTPPGQSPNRSISGKKLCSSCGLPLGKGAAMIETLNLYFHIQCFCRGICKGQLGDAVS  
GTDVRIRNGLLNCNDCYMRSR SAGQPTTL

SEQID No:286

MAARGRRRAEPQGREAPGPAGGGGGGSRWAESGSGTSPESGDEEVSGAGSSPVSGG  
VNLFANDGSFLELFKRKMEEEEQRQRQEEPPPGPQRPDQSAAAAGPGDPKRKGGPGS  
TLSFVGKRRGGNKLALKTGIVAKKQKTEDEVLT SKGDAWAKYMAEVKKYKAHQCGDD  
DKTRPLVK

SEQID No:287

MAAETQTLNFGPEWLRALSSGGSITSPPLSPALPKYKLADYRYGREEMLALFLKDNKIP  
SDLLDKEFLPILQEEPLPPLALVPFTEEEQRNFMSVNSAAVLRLTGRGGGGGTVVGAPR  
GRSSSRGRGRGRGECGFYQRSFDEVEGVFGRGGGGREMHRSSQSWEEERGDRRFEKP

GRKDVGRPNFEEGGPTSVGRKHEFIRSESENWRIFREEQNGEDEDGGWRLAGSRRD  
 GERWRPHSPDGPRSAGWREHMERRRRFEFDFRDRDDERGYRRVRSGSGSIDDDR  
 SLPEWCLEDAEEEMGTFDSSGAFLSLKKVQKEPIPEEQEMDFRPVDEGEECSDSEGSH  
 NEEAKEPDKTNKKEGEKTDVRGVEASEETPQTSSSSARPGTPSDHQSQEASQFERKD  
 EPKTEQTEKAEETRMENSLPAKVPSRGDEMADVQQPLSQIPSDTASPLLILPPPVPN  
 PSPTLRPVETPVVGAPGMGSVSTEPDDEEGLKHLEQQAEMVAYLQDSALDDERLASK  
 LQEHRAKGVSIPLMHEAMQKWYYKDPQGEIQGPFNNQEMAWEWFQAGYFTMSLLVKRA  
 CDES FQPLGDIMKMWGRVPFSPGPAPPPHMGELDQERLTRQQELTALYQMQLHQYQ  
 QFLIQQQYAQVLAQQQKAALSSQQQQQLALLLQQFQTLKMRISDQNIIPSVTRSVSPD  
 TGSIWELQPTASQPTVWEGGSVWDLPLDTTTPGPALEQLQQLEKAKAAKLEQERREAE  
 MRAKREEEERKRQEELRRQQEEILRRQQEEERKRREEEELARRKQEEALRRQREQEIA  
 LRRQREEEERQQQEEALRRLEERRRREEEERRKQEELLRKQEEEEAAKWAREEEEEAQRR  
 LEENRLRMEEEEAARLRHEEEERKRKELEVQRQKELMRQRQQQQQEALRRLQQQQQQQ  
 QLAQMKLPSSSTWGQQSNTTACQSQATLSLAEIQKLEEEERERQLREEQRRQQRELMK  
 ALQQQQQQQQQQKLSGWGNVSKPSGTTKSLEIQQEEARQMOKQQQQQQQQHQPNR  
 ARNNTHSNLHTSIGNSVWGSINTGPPNQWASDLVSSIWSNADTKNSNMGFWD DAVKE  
 VGPRNSTNKNKKELK

SEQID No:288

MVGKCLKQNLLACLVISSVTVFYLGQHAMECHHRIEERSQPVKLESTRTTVRTGLDLKA  
 NKTFAYHKDMPLIFIGGVPRSGTTLMRAMLDAHPDIRCGEETRVIPRILALKQMWSRSSK  
 EKIRLDEAGVTDEVLD SAMQAFLLEIIVKHGEPAPYLCNKDPFALKSLTYLSRLFPNAKFL  
 LMVRDGRASVHSMISRKVTIAGFDLNSYRDCLTKWNRAIETMYNQCMVEVGYKKCMLVH  
 YEQLVLHPERWMRTLKFLQIPWNHSLVHHEEMIGKAGGVSLSKVERSTDQVIKPVNV  
 GALSKWVGKIPPDVLQDMAVIAPMLAKLGYDPYANPPNYGKPDPKIENTRRVYKGEFQ  
 LPDFLKEKPQTEQVE

SEQID No:289

MSTFRQEDVEDHYEMGEELGSGQFAIVRKCRQKGTGKEYAAKFIKKRRLSSSRRGVSR  
 EEIEREVNILREIRHPNIITLHDIFENKTDVVLILELVSGGELFDFLAEKESL TEDEATQFLK  
 QILDGVHYLH SKRIAHFDLKPENIMLLDKNVPNPRIKLIDFGIAHKIEAGNEFKNIFGTPEF  
 VAPEIVNYEPLGLEADMWSIGVITYILLSGASPFLGETKQETLTNISAVNYDFDEEYFSNT  
 SELAKDFIRRLLVKDPKRRMTIAQSLEHSWIKAIRRRNVRGEDSGRKPERRRLKTTRLKE  
 YTIKSHSSLPPNNSYADFERFSKVLEEAAAAEEGLRELQRSRRLCHEDVEALAAIYEEKE

AWYREESDSLQDLRRLRQELLKTEALKRQAQEEAKGALLGTSGLKRRFSRLENRYEA  
LAKQVASEMRFVQDLVRALEQEKLGVEGCLR

SEQID No:290

MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDS DPS  
GTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR  
CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPC  
GIDKFRGVFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEE  
EEVAEVEEEEEADDDDEDDEDGDEVEEEAEOPYEEATERTTSIATTTTTTTTESVEEVVRVP  
TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKN  
LPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQ  
AVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE  
RMNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDDLANMISEPRISYGNDALMPSLT  
ETKTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGS  
GLTNIKTEEISEVNLDAAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIV  
ITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

SEQID No:291

MMHALEVLNSQETGPTLPRQNSQLPAQVQNGPSQEELEIQRRQLQEQQRQKELERER  
LERERMERERLERERLERERLERERLEQEQLERERQERERQERLERQERLERQERLE  
RQERLDRERQERQERERLERLERERQERERQEQLEREQLEWERERRISSAAAPASVE  
TPLNSVLGDSSASEPGLQAASQPAETPSQQGIVLGPLAPPPPPPLPPGPAQASVALPPP  
PGPPPPPPPLPSTGPPPPPPPPPLPNQVPPPPPPPPAPPLPASGFFLASMSEDNRPLTGL  
AAAIAGAKLRKVS RMEDTSFPSGGNAIGVNSASSKTD TGRGNGPLPLGGSGLMEEMSA  
LLARRRRRIA EKGSTIETE QKEDKGEDSEPVTSKASSTSTPEPTRKP WERTNTMNGSKSP  
VISRPKSTPLSQPSANGVQTEGLDYDRLKQDILDEM RKELTKLKEELIDAIRQELSKSNT  
A

SEQID No:292

RHTRTHRDTRHTYTHAHTDAHTCTHMHRDTQMHTHTICRKKYALTNIAAMGLSDPAA  
QPLLGNGSANIKLVKNGENQLRKAAEQGQQDPNKNLSPTAVINITSEKLEGKEPHPQDS  
SSCEILPSQPRRTKSFLNYYADLETSARELEQNRGNHHGTAEKSKPVQGGQASTIIGNG  
DLLLQKPNRPQSSPEDGQVATVSSSPETKKDHPKTGAKTDCALHRIQN LAPSD EESSW  
TTLSQDSASPSSPDETDIWSDFSQTDPDLPPGWKRVSDIAGTYYWHIPTGTTQWERP

VSIPADLQGSRKGSLSVTPSPTPENЕКQPWSDFAVLNGGKINSIDIWKDLHAATVNPDP  
 SLKEFEGATLRYASLKLRNAPHHPDDDDSCSINSIDPEAKCFAVRSLGWVEMAEEDLAPG  
 KSSVAVNNCIRQLSYCKNDIRDTVGIWGEGKDMYLILENDMLSLVDPMDRSVWHSQPIV  
 SIRVWGVGRDNGRDFAYVARDKDTRILKCHVFRCDTPAKAIATSLHEICSKIMAERKNAK  
 ALACSSLQERANVNLDVPLQVDFPTPKTEL VQKFHVQYLGMLPVDPKPVGMDILNSAIEN  
 LMTSSNKEDWLSVNMNVADATVTVISEKNEEEVLVECRVRFLSFMGVGKDVHTFAFIM  
 DTGNQRFECHEVFWCEPNAGNVSEAVQAACMLRYQKCLVARPPSQKVRPPPPPADSV  
 TRRVTTNVKRGVLSLIDTLKQKRPVTEMP

SEQID No:293

MAQVAMSTLPVEDEESSES RMVVTFLMSALESMCKELAKSKAEVACIAVYETDVFVVG  
 TERGRAFVNTRKDFQKDFVKYCVEEEEKAAEMHKMKSTTQANRMSVDAVEIETLRKTV  
 EDYFCFCY G KALGKSTVVPVPYEKMLRDQSAVVVQGLPEGVAFKHPENYDLATLKWIL  
 ENKAGISFIIKRPFLPKKHVGGRVMVTDADRSILSPGGSCGPIKVKTEPTEDSGISLEMA  
 AVTVKEESED PDYYQYNIQAGPSETDDVDEKQPLSKPLQGSHHSSEGNEGTEMEVPA  
 EDSTQHV PSETSEDPEVEVTIEDDDYSPPSKRPKANELPQPPVPEPANAGKRKVREFN  
 FEKWNARITDLRKQVEELFERKYAQAIKAKGPVTIPYPLFQSHVEDLYVEGLPEGIPFRR  
 PSTYGIPRLERILLAKERIRFVIKKHELLNSTREDLQLDKPASGVKEEWYARITKLRKMVD  
 QLFCKKFAEALGSTEAKAVPYQKFEAHPNDLYVEGLPENIPFRSPSWYGIPRLEKIIQVG  
 NRIKFVIKRPELLTHSTTEVTQPRNTNPVKEDWNVRITKLRKQVEEIFNLKFAQALGLTEA  
 VKVPYPVFESNPEFLYVEGLPEGIPFRSPTWFGIPRLERIVRGSNKIKFVVKKPELVISYL  
 PPGMASKINTKALQSPKRPRSPGSNSKVPEIEVTVEGPNNNNNPQTSAVRTPTQTNGSN  
 VPFKPRGREFSFEAWNAKITDLKQKVENL FNEKCGEALGLKQAVKVPFALFESFPEDFY  
 VEGLPEGVPFRRPSTFGIPRLEKILRNKAKIKFIIKKPEMFETAIKESTSSKSPPRKINSSP  
 NVNTTASGVEDLNIIQVTIPDDDNERLSKVEKARQLREQVNDLFSRKFGAIGMGFPVKV  
 PYRKITINPGCVVVDGMPPGVSFKAPSYLEISSMRRILDSAEFIKFTVIRPFPGLVINNQLV  
 DQSESEGPVIQESAEPSQLEVPATEEIKETDGSSQIKQEPDPTW

SEQID No:294

MAFVCLAIGCLYTFLISTTFGCTSSSDTEIKVNPPQDFEIVDPGYLGYLYLQWQPPLSLD  
 HFKECTVEYELKYRNIGSETWKTIITKNLHYKDGFDLNKGIEAKIHTLLPWQCTNGSEVQ  
 SSWAETTYWISPQGIPETKVQDMDCVYYNWQYLLCSWKPGIGVLLDTNYNLFYWYEG  
 DHALQCVDYIKADGQNIGCRFPYLEASDYKDFYICVNGSSENKPIRSSYFTFQLQNIVKP  
 LPPVYLTF TRESSCEIKLKWSIPLGPIPARCFDYEIEIREDDTTLVTATVENETYTLKTTNE



TRQLCFVVRSKVNIYCSDDGIWSEWSDKQCWEGEDLSKKTLLRFWLPFGFILILVIFVTG  
 LLLRKPNTYPKMIPEFFCDT

SEQID No:295

MAERESGGLGGGAASPPAASPFLGLHIASPPNFRLTHDISLEEFEDDLSEITDECGISL  
 QCKDTLSLRPPRAGLLSAGGGGAGSRLQAEMLQMDLIDATGDTPGAEDDEEDDDEER  
 AARRPGAGPPKAESGQEPASRGQQGQSQQGQSGDTPRKRPTTLNLFQVPRS  
 QDTLNNNSLGKKHSWQDRVSRSSSPLKTGEQTPPHEHICLSDELPPQSGPAPTDDRGT  
 STDSPCRRSTATQMAPPGGPPAAPPGGRGHSHRDRIHYQADVRLATEEIIYLTVPVQRP  
 PDAAEPTSAFLPPTESRMSVSSDPDPAAYPSTAGRPHPSISEEEEEGFDCLSSPERAEPP  
 GGGWRGSLGEPPPPPRASLSSDTSALSYDSVKYTLVVDEHAQLELVSLRPCFGDYSDE  
 SDSATVYDNCASVSSPYESAIGEYEEAPRPQPPACLSDESTPDEPDVHFSKKFLNVF  
 MSGRSRSSSAESFGLFSCIINGEEQEQTTHRAIFRFVPRHEDELELEVDDPLLVELQAED  
 YWYEAYNMRTGARGVFPAYYAIEVTKEPEHMAALAKNSDWVDQFRVKFLGVSQVPYH  
 KGNDVLCAAMQKIATTRRLTVHFNPPSSCVLEISVRGVKIGVKADDSQEAKGNKCSHFF  
 QLKNIISFCGYHPKNNKYFGFITKHPADHRFACHVFVSEDSTKALAESVGRAFQQFYKQF  
 VEYTCPTEDIYLE

SEQID No:296

GSELETAMETLINVFHAHSGKEGDKYKLSKKELKELLQTELSGFLDAQKDVDKVMK  
 ELDENGDEVDVFQEYVVLVAALTVACNNFFWENS

SEQID No:297

MASTTTCTRFTDEYQLFEELGKGAFSVVRRRCMKIPTGQGYAAKIINTKKLSARDHQKLE  
 REARICRLLKHPNIVRLHDSISEEGFHYLVFDLVTGGELFEDIVAREYYSEADASHCIQQI  
 LESVNHCHLNGIVHRDLKPENLLLASKSKGA AVKLADFGLAIEVQGDQQAWFGFAGTP  
 GYLSPEVLRKDPYGKPVDMWACGVILYILLVGYPFWDEDQHRLYQQIKAGAYDFPSP  
 EWDTVTPEAKDLINKMLTINPAKRITASEALKHPWICQRSTVASMMHRQETVDCLKKFN  
 ARRKLGAILTTMLATRNFSAAKSLLKKPDGVKESTESSNTTIEDVDKARKQEIIKVTEQ  
 LIEAINNGDFEAYTKICDPGLTAFEPEALGNLVEGMDFHRFYFENALSKSNKPIHTIILNPH  
 VHLVGDDAACIAYIRLTQYMDGSGMPKTMQSEETRVWHRRDGKWQNVHFHRSGSPT  
 VPIKPPCIPNGKENFSGGTSLWQNI

SEQID No:298

MTATEALLRVLLLLLAFGHSTYGAECFPACNPQNGFCEDDNVCRCQPGWQGPLCDQC  
 VTSPGCLHGLCGEPGQCICTDGWDGELCDRDVRACSSAPCANNGTCVSLDGGLYECS  
 CAPGYSGKDCQKKDGPCVINGSPCQHGGTCVDDEGRASHASCLCPPGFSGNFCEIVA  
 NSCTPNPCENDGVCTDIGGDFRCRCPAGFIDKTCSRPTVNCASSPCQNGGTCLQHTQ  
 VSYECLCKPEFTGLTCVKKRALSPQQVTRLPSGYGLAYRLTPGVHELPVQQPEHRILKV  
 SMKELNKKTPLLTEGQAICFTILGVLTSLVVLGTVGIVFLNKCETWVSNLRYNHMLRKKK  
 NLLLQYNSGEDLAVNIIFPEKIDMTTFSKEAGDEEI

SEQID No:299

MATIPDWKLQLLARRRQEEASVRGREKAERERLSQMPAWKRGLLERRRAKLGLSPGE  
 PSPVLGTVEAGPPDPDESAVLLEAIGPVHQNRFRIRQERQQQQQQQQQRSEELLAERKPG  
 PLEARERRPSPGEMRDQSPKGRESREERLSPRETRERRLGIGGAQELSLRPLEARDW  
 RQSPGEVGDRSSRLSEAWKWRLSPGETPERSLRLAESREQSPRRKEVESRLSPGESA  
 YQKLGLTEAHKWRPDSRESQEQSLVQLEATEWRLRSGEERQDYSEECGRKEEWPVP  
 GVAPKETAELSETLTREAQGNSSAGVEAAEQRPVEDGERGMKPTEGWKWTLNSGKA  
 REWTPRDIEAQTQKLEPPESAELLES PGVEAGEGEAEKEEAGAQQGRPLRALQNCCSV  
 PSPLPPEDAGTGGLRQQEEEAVELQPPPPAPLSPPPPAPTAPQPPGDPLMSRLFYGVK  
 AGPGVGAPRRSGHTFTVNPRRSVPPATPATPTSPATVDAAVPGAGKKRYPTAEELVL  
 GGYLRLSRSLAKGSPERHHKQLKISFSETALETYQYPSESSVLEELGPEPEVPSAPN  
 PPAAQPDDEEDEEELLLLQPELQGGGLRTKALIVDESCRR

SEQID No:300

MSEHVEPAAPGPGPNGGGGGGPAPARGPRTPNLNPINVRDRLFHALFFKMAVTYS  
 RLFPPAFRRRLFEEFFVLLKALFVLFVLAYIHIVFSRSPINCLEHVRDKWPREGILRVEVRHN  
 SSRAPVFLQFCDSGGGRGSFPGLAVEPGSNLMEDEEEEEELTMEMFGNSSIKFELDIEP  
 KVFKPPSSTEALNDSQEFPFPETPTKVWPQDEYIVEYSLEYGFLRLSQATRQRLSIPVM  
 VVTLDPTRDQCFGDRFSRLLLDEFLGYDDILMSSVKGLAENEENKGFLRNVSSEGEHYRF  
 VSMWMARTSYLAFAIMVIFTLSVSMLLRYSHHQIFVFIVDLLQMLEMNMAIAFPAAPLLT  
 VILALVGMEAIMSEFFNDTTTAFYIILIVWLADQYDAICCHTSTSKRHWLRRFFYLYHFAFYA  
 YHYRFNGQYSSLALVTSWLFIQHSMIYFFHHYELPAILQQVRIQEMLLQAPPLGPGTPTA  
 LPDDMNNNSGAPATAPDSAGQPPALGPVFELVSKERGWGSAEGSGGVLVGLQ

SEQID No:301

KEQSELDQDLDDVEEVEEEEETGEETKLKARQLTVQMMQNPQILAAALQERLDGLVETPT  
 GYIESLPRVVKRRVNALKNLQVKCAQIEAKFYEEVHDLERKYAVLYQPLFDKRFEIINAIY  
 EPTEECEWKPDEEDEISEELKEKAKIEDEKKDEEKEDPKGIPFWLTVFKNVDLLSDM  
 VQEHDEPILKHLKDIKVKFSDAGQPMSFVLEFHFEPNEYFTNEVLTKTYRMRSEPDDSD  
 PFSFDGPEIMGCTGCQIDWKKGKNVTLKTIKKKQKHKGRTVVRTVTKTVSNDSEFFNFFA  
 PPEVIPKFSADFDDAEAILAADFEIGHFLRERIIPRSVLYFTGEAIEDDDDDYDEEGEEAD  
 EGYQLFEEVKSCSKLFQRWLQ

SEQID No:302

GKQNSKLRPEVMQDLLESTDFTEHEIQEWYKGFLRDCPSGHLSMEEFKKIYGNFFPYG  
 DASKFAEHVFRTFDANGDGTIDFREFIALSVTSRGKLEQKLKWAFSMYDLGNGYISKA  
 EMLEIVQAIYKMVSSVMKMPEDSTPEKRTEKIFRQMDTNRDGKLSLEEFIRGAKSDPSI  
 VRLQCDPSSAGQF

SEQID No:303

MVEKGPEVSGKRRGRNNAASASAAAASAAASAACASPAATAASGAAASSASAAAAS  
 AAAAPNNGQNKSLAAAAPNGNSSNSWEEGSSGSSSDEEHGGGGMRVGPQYQAVV  
 PDFDPAKLARRSQERDNLGMLVWSPNQNLSEAKLDEYIAIAKEKHGYNMEQALGMLFW  
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 YSWKKTRTKTSVMDRHARKQKREREESEDELEEANGNNPIDIEVDQNKESKKEVPPT  
 TVPQVKKEKHSTQAKNRAKRKPPKGMFLSQEDVEAVSANATAATTVLRQLDMELVSVK  
 RQIQNIKQTNSALKEKLDGGIEPYRLPEVIQKCNARWTTEEQLLAVQAIRKYGRDFQAIS  
 DVIGNKSVVQVKNFFVNYRRRFNIDEVLQEWAEHKGKEETNGPSNQKPKSPDNSIKM  
 PEEEDEAPVLDVRYASAS

SEQID No:304

MSELEKAMVALIDVFHQYSGREGDKHKLKKSELKELINNELSHFLEEIKEQEVVDKVMET  
 LDNDGDGECDFQEFMAFVAMVTTACHEFFEHE

SEQID No:305

MDDDIAALVVDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMMVGMGQKDSYVGD  
 EAQSKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANR  
 EKMTQIMFETFNTPAMYVAIQAVLSLYASGRTTGIVMDSGDGVTHTVPIYEGYALPHAIL

RLDLAGRDLTDYLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMATAASSSSL  
 EKSYPELDGQVITIGNERFRCPEALFQPSFLGMESCGIHETTFNSIMKCDVDIRKDLYAN  
 TVLSGGTTMYPGIADRMQKEITALAPSTMKIKIIAPPERKYSVWIGGSILASLSTFQQMWI  
 SKQEYDESGPSIVHRKCF

SEQID No:306

MRECISIHVGQAGVQIGNACWELCYCLEHGIQPDGQMPSDKTIGGGDDSFNTFFSETGA  
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 DRIRKLADQCTGLQGFLVFHSFGGGTGSGFTSLLMERLSVDYGGKSKLEFSIYPAPQVS  
 TAVVEPYNSILTTHHTTLEHSDCAFMVDNEAIYDICRRNLDIERPTYTNLNLRLISQIVSSITA  
 SLRFDGALNVDLTEFQTNLVPYPRIHFPLATYAPVISAEEKAYHEQLSVAEITNACFEPAN  
 QMVKCDPRHKGKYMACECLLYRGDVVPKDVNAAIATIKTKRSIQFVDWCPTGFKVGINYQ  
 PPTVVPGGDLAKVQRAVCMLSNTTAIAEAWARLDHKFDLMYAKRAVHWYVGEEMEE  
 GEFSEAREDMAALEKDYEEVGVDSEGEGEEEEGEEY

SEQID No:307

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 DVVRKEAESCDCLQGFQLTHSLGGGTGSGMGTLISKIREEYPDRIMNTFSVVPSPKVS  
 DTVVEPYNATLSVHQLVENTDETYCIDNEALYDICFRTLKLTPTTYGDLNHLVSATMSGV  
 TTCLRFPQQLNADLRKLAVNMVPPRLHFFMPGFAPLTSRGSQQYRALTVPELTQQVF  
 DAKNMMAACDPRHGRYLTVAAVFRGRMSMKEVDEQMLNVQKNSSYFVEWIPNNVK  
 TAVCDIPPRGLKMAVTFIGNSTAIQELFKRISEQFTAMFRRKAFLHWYTGEGMDEMEFT  
 EAESNMNDLVSEYQQYQDATAEEEEEDFGEEAEEEA

SEQID No:308

MEGSLEREAPAGALAAVLKHSSTLPPESTQVRGYDFNRGVNYRALLEAFGTTGFQATN  
 FGRAVQQVNAMEKKLEPLSQDEDQHADLTQSRRPLTSCTIFLGYSNLISSGIRETIRYL  
 VQHNMDVVLVTTAGGVEEDLIKCLAPTYLGEFSLRGKELRENGINRIGNLLVPNENYCKF  
 EDWLMPILDQMVMEQNTEGVKWTPSKMIARLGKEINNPESVYYWAQKNHIPVFSPALT  
 DGSLGDMIFFHSYKNPGLVLDIVEDLRLINTQAIFAKCTGMILGGGVVKHHIANANLMRN  
 GADYAVYINTAQEFDGSDSGARPDEAVSWGKIRVDAQPVKVYADASLVFPLLVAETFA  
 QKMDAFMHEKNED



SEQID No:309

MADPKYADLPGIARNEPDVYETSDLPEDDQAEFDAAEELTSTSVEHIIVNPNAAYDKFKDK  
 RVGTKGLDFSDRIGKTKRTGYESGEYEMLGEGLGVKETPQQKYQROLLHEVQELTTEVE  
 KIKTTVKESATEEKLTPVLLAKQLAALKQQLVASHLEKLLGPDAAINLTDPDGALAKRLLL  
 QLEATKNSKGGSGGKTTGTPPDSSLVTYELHSRPEQDKFSQAAKVAELEKRLTELETA  
 VRCDQDAQNPLSAGLQGACLMETVELLQAKVSALDLAVLDQVEARLQSVLGKVNEIAK  
 HKASVEDADTQSKVHQLYETIQRWSPIASTLPELVQRLVTIKQLHEQAMQFGQLLTHLD  
 TTQQMIANSLKDNTLLTQVQTTMRENLATVEGNFASIDERMKKLGK

SEQID No:310

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 VSKFCKYEHDDIVSTVSVLSSGTQAVSGSKDICKVWDLAQQVVLSSYRAHAAQVTCVA  
 ASPHKDSVFLSCSEDNRILLWDTRCPKPASQIGCSAPGYLPTSLAWHPQQSEVFVFGD  
 ENGTVSLVDTKSTSCVLSSAVHSQCVTGLVFSPHSVPFLASLSEDCSLAVLDSSLSELF  
 RSQAHRDFVRDATWSPLNHSLLTTVGWDHQVVHHVVPTEPLPAPGPASVTE

SEQID No:311

MSISSDEVNFLVYRYLQESGFSHSAFTFGIESHISQSNINGALVPPAALISIIQKGLQYVEA  
 EVSINEDGTLFDGRPIESLSLIDAVMPDVVQTRQQAYRDKLAQQQAAAAAAAAAAAAASQQ  
 GSAKNGENTANGEENGAHTIANNHTDMMEVDGDVEIPPKNKAVVLRGHESEVFICAWNP  
 VSDLLASGSGDSTARIWNLSNSTSGSTQLVLRHCIREGGQDVPSNKDVTSLDWNSEG  
 TLLATGSYDGFARIWTKDGNLASTLGQHKGPFIKWKWNKKGNFILSAGVDKTTIIWDAHT  
 GEAKQQFPFHSAPALDVDWQSNNTFASCSTDMCIHVCKLGQDRPIKTFQGHTNEVNAI  
 KWDPTGNLLASCSDDMTLKIWSMKQDNCVHDLQAHNKEIYTIKWSPTGPGTNNPNANL  
 MLASASFDSTVRLWDVDRGICHTLTKHQEPVYSVAFSPDGRYLASGSFDKCVHIWNTQ  
 TGALVHSYRGTTGGIFEVCWNAAGDKVGASASDGSVCVLDLRK

SEQID No:312

MDEKVFTKELDQWIEQLNECKQLSESQVKSLCEKAKEILTKESNVQEVRCPTVCGDV  
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 HESRQITQVYGFYDECLRKYGNANVWKYFTDLFDYLPLTALVDGQIFCLHGGLSPSIDTL  
 DHIRALDRLQEVPHGPMCDLLWSDPDDRGGWGISPRGAGYTFGQDISETFNHANGL

TLVSRAHQLVMEGYNWCHDRNVVTIFSAPNYCYRCGNQAAIMELDDTLKYSFLQFDPA  
PRRGEPHVTRRTPDYFL

SEQID No:313

MDDKAFTKELDQWVEQLNECKQLNENQVRTLCEKAKEILTKESNVQEVRCPTVTVCGDV  
HGQFHDLMELEFRIGGKSPDTNYLFMGDYVDRGYYSVETVTLLVALKVRYPERITILRGN  
HESRQITQVYGFYDECLRKYGNANVWKYFTDLFDYLPLTALVDGQIFCLHGGLSPSIDTL  
DHIRALDRLQEVPHEGPMCDLLWSDPDDRGGWGISPRGAGYTFGQDISETFNHANGL  
TLVSRAHQLVMEGYNWCHDRNVVTIFSAPNYCYRCGNQAAIMELDDTLKYSFLQFDPA  
PRRGEPHVTRRTPDYFL

SEQID No:314

AAADGDDSLYPIAVLIDELRNEDVQLRLNSIKKLSTIALALGVERTRSELLPFLTDTIYDED  
EVLALAEQLGTFTTLVGGPEYVHCLLPPLSLATVEETVVRDKAVESLRAISHEHSPSD  
LEAHFVPLVKRLAGGDWFTSRTSACGLFSVCYPRVSSAVKAELRQYFRNLCSDDTPMV  
RRAAASKLGEFAKVELDNVKSEIIPMFSNLASDEQDSVRLlaveACVNIAQLLPQEDLE  
ALVMPTLRQAAEDKSWAVRYMVADKFTTELQKAVGPEITKTDLPVAFQNLMKDCEAEVR  
AAASHKVKEFCENLSADCRENVIMSQILPCIKELVSDANQHVKSALASVIMGLSPILGKD  
NTIEHLLPLFLAQLKDECPEVRLNIISNLDVNEVIGIRQLSQSLLPAIVELAEDAKWRVRL  
AII EYMP LLAGQLGVEFFDEKLNSLCMAWLVDHVYAIREAATSNLKKLVEKFGKEWAHA  
TIIPKVLAMSGDPNYLHRMTTLFCINVLSEVCGQDITTKHMLPTVLRMAGDPVANVRFNV  
AKSLQKIGPILDNSTLQSEVKPILEKLTQDQDQDVVKYFAQEALTVLSLA

SEQID No:315

MAEPRQEFVMEFHAGTYGLGDRKDQGGYTMHQDQEGD TDAGLKESPLQTPTEDGS  
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DEAAGHVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPPGQKGQANATRIP  
AKTPPAPKTPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPTREP KKVAVVR  
TPPKSPSSAKSRLQTAPVPMPDLKNVKS KIGSTENLKHQP GGGK VQIINKKLDLSNVQS  
KCGSKDNIKHVP GGGSVQIVYKPV DLSKVT SKCGSLGNIH HKPGGGQVEVKSEK LDFK  
DRVQSKIGSLDNITHVP GGGGNKKIETHKLT FREN AKAKTDHGAEIVYKSPVVSGDTS PR  
HLSNV SSTG SIDMVDSPQLATLADEV SASLAKQGL



**CLAIMS**

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
  - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm



DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;  
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

5. The complex of any of Claim 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of Claim 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of Claim 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of Claim 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of Claim 1 - 8 and optionally the components thereof comprising the following steps:  
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to Claim 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of Claim 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of Claim 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a

functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to Claim 13.
15. Construct, preferably a vector construct, comprising
  - (a) a nucleic acid according to Claim 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
  - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to Claim 1 (a) and at least one of said proteins, being selected from the second group of proteins according to Claim 1 (b) or
  - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to Claim 1.
16. Host cell, containing a vector comprising at least one nucleic acid of Claim 14 and /or a construct of Claim 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to Claim 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to Claim 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of

Claim 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to Claim 13.

18. A kit comprising in one or more containers:

- (a) the complex of any of Claim 1 - 8 and/or the proteins of Claim 13 and/or
- (b) an antibody according to Claim 17 and/or
- (c) a nucleic acid encoding a protein of the complex of any of Claim 1 - 8 and/or a protein of Claim 13 and/or
- (d) cells expressing the complex of any of Claim 1 - 8 and/or a protein of Claim 13 and, optionally,
- (e) further components such as reagents, buffers and working instructions.

19. The kit according to Claim 18 for processing a substrate of a complex of any one of Claim 1 - 8.

20. The kit according to Claim 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.

21. Array, preferably a microarray, in which at least a complex according to any of Claim 1 - 8 and/or at least one protein according to Claim 13 and/or at least one antibody according to Claim 17 is attached to a solid carrier.

22. A process for modifying a substrate of a complex of any one of Claim 1 - 8 comprising the step of bringing into contact a complex of any of Claim 1 - 8 with said substrate, such that said substrate is modified.

23. A pharmaceutical composition comprising the protein complex of any of Claim 1 - 8 and/or a protein according to Claim 13.



24. A pharmaceutical composition according to Claim 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of Claim 1 - 8 and/or a protein of Claim 13, comprising the following steps:
- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of Claim 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
  - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of Claim 26, wherein the amount of said complex is determined.
28. The method of Claim 26, wherein the activity of said complex is determined.

29. The method of Claim 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of Claim 26, wherein the amount of the individual protein components of said complex is determined.
31. The method of Claim 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of Claim 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of Claim 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of Claim 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the Claim 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of Claim 35, wherein the amount of said complex is determined.
37. The method of Claim 35, wherein the activity of said complex is determined.
38. The method of Claim 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of Claim 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of Claim 39, wherein said determining step comprises determining whether any of the proteins according to Claim 13 is present in the complex.
41. The complex of any one of Claim 1 - 8, or a protein of Claim 13 or an antibody or fragment thereof of Claim 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of Claim 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to Claim 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to Claim 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of Claim 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.



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